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CANCER AND WATER

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CANCER AND WATER

A STUDY OF THE NATURE, CAUSATION, AND PREVENTION OF CANCER

JAMES W. SHANNON, M. B.

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Cancer and Water

PART I

The progressive increase of cancer is a subject which, of late years, has attracted the attention of most thoughtful persons to the question of how best to protect the community from its attack. To attain this object no effort or expense has been spared, and no advantage of modern science or organization neglected; yet, it must be confessed, the results of all these endeavors are far from satisfying or their promise for the future hopeful.

Medical theory and modern methods of investigation have progressed to a point where it is possible, in many cases, not only to define with exactness the exciting cause of a disease, but also to form clear conceptions of some of the principles underlying its manifestations, and deductions of considerable accuracy concerning its prevention and cure. In other cases, even though the actual cause of a disease is still undiscovered, it is nevertheless possible by analogy to infer its true nature, and from the deductions thus reached to devise correct methods for its prevention. The cause of yellow-fever, for example, is uncertain, but by the application of theoretical principles the disease has virtually ceased to exist in places where heretofore it was never absent. In view of the results already achieved it must be conceded that the Science of Medicine is entitled to claim a very considerable degree of exactness, and though there are many matters which are still obscure, it cannot be doubted

that with further progress it will be possible to explain the majority of them on the basis of the principles already established.

Neoplasms are unexplainable by existing theories.—It would appear that an exception to the foregoing must be made with regard to those diseases which pathologically are grouped together under the term "Neoplasms" or "New-Growths." A review of the chemical and pathological features which are common to this group cannot fail to show that it has no relation to any other class of disease, and it is therefore not a matter for surprise that the principles which have been established by a study of other diseases when applied to new-growths should be found totally inadequate to explain their phenomena. New-growths are in fact beyond the range of existing theories of disease, and no true progress is possible with respect to them without theoretical developments in a new direction.

Normal, Benign and Malignant Growth is identical in nature, but differs in degree.—The distinction between benign and malignant new-growths is based upon certain clinical features, and not upon any essential difference in composition or structure of the growths themselves. Even clinically the distinction is not always clearly marked: a benign growth develops slowly, a malignant one rapidly, but between the extremes there is a middle region where it is impossible to distinguish one class from the other. It is also impossible to make a fundamental distinction between a new-growth and the normal tissues of corresponding type: everything points

to the fact that a new-growth is composed of the same protoplasmic elements as the body in which it grows, and that it is morphologically identical with corresponding normal structures. Biologically, a new-growth is adapted to the metabolic conditions of the body as perfectly as any normal part, and reacts in a similar manner to pathological stimulation.

New-growths are not parasitic.—In two respects, neither of which are fundamental, a new-growth differs from normal structures: firstly, it develops without regard to the design of the body, and, secondly, it serves no useful purpose. Since it is dependent, in the same manner, for example, as a limb, upon the nutritive mechanisms of the body, and lives at their expense without contributing anything to the general economy, it may, in a broad sense, be considered parasitic. In a strict sense, however, a new-growth is not a true parasite. A parasite derives its nourishment from its host, but it possesses its own vital mechanisms which are independent of, and different from, those of the host. A parasite may die when the host dies, but it is the ancestor of successive generations which repeat its life-history in other hosts. A new-growth may be transplanted, while living, to another host, or by metastasis to other parts of the original host, but it never gives rise to a new generation: it dies when the host dies and cannot be revived.

New-growths cannot arise from an external source. Increased potency is their chief fundamental characteristic.—The facts that a new-growth is biologically identical with corresponding normal tissues, and that it is

not parasitic in nature, are sufficient to exclude the possibility of its origin from a source external to the body. We are, therefore, forced to conclude that a new-growth arises from normal tissues, and is in fact a development of original elements of the body. Proof of this is seen in the fact that in reproduction every cell must "breed true", that is, it cannot give rise to cells which are not of its own type. When it is considered that not only do the cells of a new-growth "breed true", but also that they are always of a type which is identical with the normal cells at the site of their origin, it is not possible to doubt that they are directly descended from such normal cells. There are many varieties of new-growth each having a distinct type of cells which is always identical with the normal cells of the part where it arises, and it is inconceivable that cells or organisms from a foreign source, planted in the tissues by chance, should invariably correspond with the type of cells among which they happen to fall.

Accepting, then, the view that the parent of the cells of a new-growth, is one or more cells which were originally normal, it becomes necessary to consider the reasons for its irregular reproductive activity. For the sake of clearness it is desirable at present to limit this part of the subject to certain general considerations, reserving its full discussion until later.

Vital energy is the only form of force capable of inducing reproduction or growth.—We are ignorant of the ultimate nature of any form of energy, but by observations of its manifestations through matter, we have

gained, among other things, the knowledge that its operations are uniform, unchangeable, and infinitely exact. The laws of Science have been established upon observations of sufficient completeness, and though they cover only a small portion of the total known and unknown facts, yet their logical force is so great that it is not possible to doubt that every manifestation is governed by a uniform principle or law.

Physical Science deals with simple or elementary forms of matter, and it is possible to demonstrate the uniformity of action of natural forces with mathematical exactness; Biology is concerned with protoplasm, which is a form of matter so infinitely complex that it will probably always defy analysis, and since the special or vital manifestations of energy in protoplasm is largely a matter of molecular changes, the difficulties of observations and the impossibility of reducing them to the form of scientific laws will be readily understood. It cannot be doubted, however, that the laws which govern the action of vital energy in protoplasm are less rigid than those which regulate physical energy in elementary matter, not only for the general reasons already discussed, but also on the ground that a consideration of the distinctions maintained between the enormous number of biological species, and the conformity of each individual to the ancestral type, is a satisfying proof of the uniformity of vital phenomena.

Energy appears under many forms, such as heat, chemical action, electricity, etc., each of which may be converted into the other. There are reasons, therefore,

to conceive that the ultimate nature of all is the same, and that the form in which energy appears is determined by the kind and condition of matter in which it acts. Vital energy can only act in protoplasm, but there is no reason to believe that it differs in any essential respect from other forms of energy. It would seem to be very closely allied to chemical action, and like it may be transformed into heat, electricity, dynamic energy or other forms of force. The atom is the unit of elementary matter, and the unicellular organism or cell is the unit of protoplasmic matter, and just as an atom theoretically contains all the potentialities of the element to which it belongs, so the unicellular organism contains all the potentialities of its species, and in each case the potentialities are fixed and cannot be increased or diminished. An atom cannot act otherwise than according to its affinities, nor a unicellular organism to its nature, and the result of such action never varies; an atom of oxygen cannot combine with two atoms of hydrogen to produce any other substance than water, and similarly an organism cannot function to produce any result which is contrary to its nature. Applying the foregoing considerations to the problem of new-growth, it is evident that they are the *inevitable and only possible result* of the regular operation of that form of force which we recognize as vital energy.

A new-growth is composed of cells, each of which may be regarded as an independent organism, or biological unit, adapted to the special conditions of environment existing in the body of its host, and functioning therein

according to its species. Although it possesses all the potentialities normal to its kind, the degree to which it is able to exercise them is determined by the requirements of the body to which it belongs, and, notably in the case of the reproductive functions, by the opportunities which present themselves. It must frequently happen, then, owing to the absence of demand or opportunity, that some of the potentialities of a cell remain wholly or partially latent, but ready to respond to the full extent to increased demand or suitable conditions. It is certain, for instance, that, on the one hand, the growth of an animal may be retarded or impaired, locally or generally, by various adverse circumstances; and, on the other hand, that under appropriate condition and suitable stimulation, both local and general growth may be encouraged to the full degree. It must be clearly understood, however, that growth of this kind, occurring in accordance with the physiological requirements of the body, *can never give rise to a pathological formation.*

New-growths can only arise as the result of fertilization.—Having emphasized the fact that the origination of a new-growth must be compatible with the regular operations of vital energy, and having excluded physiological growth as a factor in its causation, it becomes impossible to evade the conclusion that it can only occur as the result of fertilization.

At the outset it may be pointed out that *fertilization is the only form of stimulation which is potent to cause growth of any kind*: and that its action is always

manifested in the form of *new growth*. Within the limits of our present knowledge of its nature, it may be defined as the reproductive stimulus following the union of the nuclei of male and female organisms, and resulting in the creation of a new individual of the same species as the female parent.

Although our knowledge of the mechanisms of fertilization and reproduction, owing to the difficulties of investigation, is very incomplete, yet it is sufficient to convince us that they are primary functions, and supreme in importance to all others. Consequently, it cannot readily be supposed that an organism which is endowed with all other functions, should be deprived of the biologically fundamental faculty of reproduction.

The processes of reproduction are designed for the continuance of the species, and hence are of the utmost concern to the future generations, and only of minor importance to existing individuals. The exercise of its reproductive functions is not necessary to the health or life of an existing organism, and it not infrequently happens that no demand arises to call them into action. Also in some species, the reproductive functions are active in comparatively few of its members, remaining latent, but not absent, in the others. A highly-evolved animal may be theoretically regarded as a combination of a large number of species of cells or organisms, each endowed with certain special functions necessary in the economy, and arranged in accordance with, the design of the animal as a whole. Although a cell has acquired special powers for the work it is required to perform,

and is unable, owing to its environment, to use certain other faculties, there is no reason to assume that it has lost them, but, in the case of the fundamental functions, many reasons to believe the contrary. In highly organized animals, certain cells, specialized like the others according to their function, are differentiated for the purpose of fertilization and reproduction. In a manner which in principle is identical with the reproduction of all living forms, the process consists in the union of a male with a female cell-organism, and the result is not only the reproduction of other organisms similar to themselves, but also of many other species of organisms which in combination constitute the whole animal. In other words, a fertilized ovum is a unicellular organism *specially* endowed with reproductive powers, by virtue of which it reproduces not only its own life history but also that of the animal of which it is a part.

Since the power of fertilization and reproduction are primary essentials of life, it follows as a necessary consequence that every living organism must possess male or female potencies. Every cell in the body of an animal is, therefore, male or female. For the present purpose, it is not necessary to discuss the considerations relating to the distinctions in sex of the cells of the body: it is sufficient only to notice the fact, which applies not only to body-cells, but also to all other organisms—that *male organisms always remain single*: *only female organisms are capable of division.* Those cells, then, of the body which are known to have had the power of division must be considered as female in nature, and

therefore capable of being fertilized by a male organism, and of reproducing after fertilization new cells of their own type. Those cells which never divide must be considered to have male qualities, and as they are the characteristic elements in nervous tissues it is of great significance to find that *they never give origin to new-growths.* New-growths may arise in the connective tissues of the brain and other nervous structures, but have *never been known to originate from the nerve-cells.*

Theoretically, then, we may consider, that only those cells which are known to be capable of division, and which, therefore, are of female nature, can develop in such a manner as to form new-growths. A review of the histological features of the tissues of the body will show that these cells are the characteristic elements of those structures which form the framework of the body, of glandular organs, and of the internal and external body-coverings. It is from these structures that new-growths take their origin.

The facts concerning muscular tissues and the blood are not sufficiently complete to justify dogmatic statements; as far as they are known, however, they are not in disagreement with, and in some directions even add support to the views already advanced. Muscle-cells are of two kinds: striped and unstriped. For the reason that they do not appear to divide, striped muscle-cells are probably of male nature, and in this connection their relation to the central nervous system is of some significance. The striped muscles are the end organs of

the important efferent or motor division of the central nervous system, and their connection with the appropriate nerve centers is more direct and intimate than in the case of any other organ. By means of direct efferent stimuli the striped muscles give effect to the ideas which have been conceived by the brain, and functionally at any rate, but probably structurally also, it would seem that the striped muscles are a part of the central nervous system.

True new-growths of striped muscle are so extremely rare that it may be permissible to doubt their occurence. It is suggested that those cases which have been observed, are due to congenital developmental irregularities, and in a strict sense are, therefore, not *new*-growths. In an article on Tumors, Dr. Rickman J. Godlee states that striped muscle has been found in certain *congenital* tumors connected with the kidney, and in a fatty tumor *within the spinal canal.*

The considerations which apply to unstriped muscle are of a different order. It may be pointed out that unstriped muscle is not directly connected with the central nervous system, but is under the influence of the sympathetic system, and no very clear conclusions are possible concerning the sex of unstriped muscle-cells. Mixed new-growths containing unstriped muscle and fibrous tissue are found with moderate frequency nearly always in connection with the uterus.

If the blood is regarded as a tissue, those diseases which are included in the term "Leukemia" may be

considered as new-growths. Leukemic diseases are characterized by an increase or overgrowth, often enormous, of certain nucleated cells of the blood or ancillary glandular organs. The increase of the type of cells affected is progressive, and corresponds in every fundamental particular with the increase of cells in a new-growth of the solid tissues, and it would seem that there is no sufficient reason to prevent them from being placed in the same division in the plan of classification. In view of the fact already considered, that new-growths can only arise from *nucleated* cells, it is of great significance to find that the red cells of the blood, which are *non-nucleated,* are never affected in such a manner as to cause an abnormal increase in their numbers.

From the foregoing it is evident that the general theoretical considerations which apply to all forms of life coincide with, and supply a consistent explanation of the essential facts of new-growths, established by observation. It is also clear that attempts to solve the problem of new-growths along the lines which have led to successful results in other diseases are foredoomed to failure. The phenomena of new-growths are of a different order to those of other diseases, and in many respects are the antithesis of disease: new-growths are generative and constructive, and the idea of repair is incongruous in connection with them, since, in a strict sense, they cause no direct or primary injury: disease is degenerative and destructive, and excites a reaction of the body and tissues for the purpose of repairing and neutralizing its effects. Such radical contrasts render

it difficult to conceive that the causes which are operative in the one case can also be active in the other. Therefore, in seeking for the cause of new-growths it is desirable to proceed along the lines indicated by a study of their nature, rather than to concentrate attention upon matters which, though valuable in other respects, are of doubtful applicability.

In continuation of the subject of the suggested causative relation of fertilization to new-growths, there is no reason to believe that the stimulus of fertilization is generated within the tissues themselves. A study of the circumstances under which new-growths, especially of the malignant type arise, and the parts of the body which they commonly select will show with reasonable certainty that the determining factors in the causation are local, not general, in their influence. In the absence of satisfying reasons to the contrary, it is justifiable to assume that a general stimulus would act equally in every part of the body, and on this basis it would be difficult to comprehend why malignant new-growths should appear three times more frequently in the stomach than in any other organ, or why the lungs should be affected with extreme rarity; why X-ray operators, paraffin and pitch workers, should be attacked in the hands, women in the breast and uterus, or chimney-sweeps in the scrotum, and so forth. Reasons, embracing these and all similar cases, consistent with the general facts of new-growths, will develop later; for the present it is sufficient to establish the point that the causative stimulus is local in its action.

The coverings of the body, if intact, are an efficient protection against the action of a fertilizing agent.— The surfaces of the body which are exposed to external influences are composed of epithelial cells which have lost their vitality, and are therefore incapable of responding to any form of stimulus. Their function is to cover and protect the living cells beneath from contact with the outer world, and *under normal conditions there is no exposure of living cells on either the internal or external surfaces of the body.* This fact is of cardinal importance in the causation of new-growths, not only on account of its theoretical significance but also because it supplies the true reason for the adoption of certain measures of protection. Guided by observation and experience only, authorities have insisted upon the necessity of caring for those lesions of the skin and mucus membranes which are embraced in the term "precancerous" or "chronic irritation", and which have been proved to be predisposing causes of malignant new-growths. The explanation depends upon the fact that as fertilization is only possible with living cells, it cannot occur if the outermost layers of the skin and mucous membranes are intact. When by injury or disease the protecting epithelium is removed sufficiently to expose the living cells beneath, even to an extent which is microscopic in size, it then becomes possible for a fertilizing agent to gain access to them, and quicken them into abnormal reproductive activity. It is, however, misleading to suppose that the action of a fertilizing agent is limited to the cells at the point of its entrance.

Similarly to any other microscopic organism, a fertilizing agent may be carried in the lymph or blood-stream to any part of the body. Its destination is, therefore, largely a matter of chance; it may unite with any type of female cell and so give rise to a new-growth of corresponding type. Thus it is possible to understand the reason for the varieties of new-growth and for the conformity of each with the tissues in which it grows: and also to realize that a new-growth is a new creation in a sense as real as that in which an embryo may be considered a new individual.

In connection with the protective function of the dead layer of epithelium of the skin, it is interesting to notice that the resemblance between simple papillomata and malignant epithelial new-growths, has been a subject of frequent remark: both are epithelial new-growths, and except for the fact that one grows inwards, and the other outwards, it is difficult to discover in what fundamental respect they differ. Further, it is significant that, in certain occupations, the skin of the parts exposed to the action of paraffin, tar, and other substances, becomes affected by warty growths, apparently benign, which precede and are associated with the epithelial growths of a malignant character. From this it would appear that both benign and malignant growths are due to the same cause, and arise under the same conditions.

The rarity of malignant growths in children is notorious, but they are affected, probably more frequently than adults, with benign papillomata of the skin. If, then, benign and malignant growths arise from the same

cause and conditions, it becomes a problem to discover a reason for the fact that new-growths are prone to assume a benign type in young persons, and a malignant form in old people. The tissues of a child are not less vulnerable, but, on account of their delicacy, probably more readily wounded by slight accidents than those of an adult; and there is no reason to believe that the action of a fertilizing agent upon the tissue-cells of a child differs from its action upon the tissue-cells of an older person. There is, however, an enormous difference in the capacity for repair, and it is to this that we must look for an explanation of the comparative immunity from malignant manifestations which young persons enjoy.

It may be supposed that, in the case of a child, there is a large reserve of vital energy which is available in the future, not only for the growth and maintenance of the body, but also for resisting and repairing the effects of deleterious influences. In the case of an old person, the reserve is exhausted, and, though for a time the body may be maintained in an apparently normal manner, resistance and repair can only be effected at the expense of the remaining store of vital energy, which is already only barely sufficient for normal needs. By the lapse of time a point is reached when there is not sufficient vital energy to maintain the tissues in a healthy and vigorous condition, and it is then that those changes appear which are recognized as senile degeneration. If it is realized that in an old person there is not sufficient energy to maintain the tissues in a normal state, it will

be readily understood that the repair of injuries can only be accomplished with difficulty, and that the process will be slow, and in some degree imperfect. There will also be a diminished power of resistance to wear and tear or strain in those parts of the body which are subjected in a greater degree to the stress of natural, morbid, occupational, or other influences, and it is to be expected that in such parts the manifestations of senility will soonest appear, and in the most pronounced form. There are a large number of senile pathological changes which are important with respect to new-growths, for the reason that they cause breaches or lesions of the internal or external protective coverings sufficient to expose living tissue-cells, and allow access to them of a fertilizing agent.

Double force is added to the foregoing considerations by the fact that they are consistent with the high degree of immunity from malignant growths associated with young persons. In children there is no predisposition to degenerative lesions, and lesions resulting from injury are quickly and perfectly repaired: consequently, the opportunities for access to the tissue-cells of a fertilizing element is reduced to a minimum. In explanation of the fact already mentioned, that benign papillomata are common in children, it is suggested that they arise by fertilization of the most superficial layers of the living cells of the skin, at the site of slight traumatisms, just sufficient to remove the epidermis and expose the cells immediately underlying it. These cells are about to become lifeless and to pass into the epidermis, and may

therefore be regarded as the senile members of the cell-community of the skin. It is probable, therefore, that they have little or no power remaining to repair the effects of injuries, and consequently afford longer opportunity for the action of a fertilizing agent than the vigorous cells of the deeper strata.

Since, owing to the nature of their function, changes appear earlier, and are more pronounced in the organs of the reproductive system than in other parts of the body, cessation of reproductive activity is followed by rapid atrophy of the parts concerned, which, similarly to other senile changes, is associated with a diminished supply of vital energy. By their situation these organs are protected in a special degree from injury and exposure to undue influences, yet notwithstanding this they are extraordinarily liable to the development of new-growths, benign and malignant, hence, with respect to them, the predisposing influences of senility are strongly accentuated. It is significant to find that those parts of the body which undergo degeneration in the fullest degree, are also disproportionately subject to the development of new-growth, and, in view of these facts, there is no room to doubt that a positive causative relation is constantly present between them.

The influence of Heredity on new-growths.—Indirectly, there is a basis for the supposition that a hereditary predisposition favors the formation of malignant new-growths. It is well known that the period of the onset of senility varies in different individuals, and it is generally recognized that such variation is determined

by the hereditary powers of resistance to environmental conditions. The tissues of those who inherit abundant vitality will resist for a long time, whereas in those of feeble powers they will tend early to develop lesions, and other evidences of senile degeneration. It will appear later that a lesion is one of four essential factors in the causation of malignant new-growths, and, therefore, new-growths may be considered remotely hereditary, in so far as they are due to the hereditary lesion which precedes them: or, in other words, *new-growths are never directly hereditary, but the lesions essential to their causation often are.*

It has already been stated that all growth is of the same fundamental nature, and that the terms "benign" and "malignant" have no reference to the principles, but only to the degree, of growth: there is no logical reason, therefore, to concentrate attention upon any particular group of manifestations to the exclusion of the others. For convenience, however, since the greater includes the less, and for the reasons that the general and statistical facts of malignant new-growths are sufficiently voluminous and authentic to afford a safe basis for sound conclusions, and also because the strongly-marked features of malignant degrees of growth exemplify more strikingly the relation of certain factors to its causation, it is desirable, from this point onwards to treat the subject with reference mainly to the facts of malignant growth. In the following, the term "Cancer" will be considered as signifying a malignant degree of growth, and as including all forms without reference to type.

The Nature of Cancer.—Cancer is a growth of cells, morphologically identical with normal cells, which develops irregularly, and without regard to the orderly arrangement of the tissues, or the functions of the body in which it grows. It is dependent upon its host only in the sense that it is suited to the environmental conditions which are present in the body, and that it derives its nourishment from the common supply: but it is *independent* of those laws of the body which regulate the manner and degree of growth in normal structures.

From the view-point of the normal cell-communities, cancer may be regarded as a vigorous colony of outlaws or rebels living at the general expense without contributing anything in return, increasing rapidly, and sufficiently powerful to invade the tissue boundaries and destroy those normal cells which happen to lie in the path of its encroachments.

Cancer-cells, then, must be considered as members of the same species as normal cells, but differing from them in their attitude towards the government of the body, and since it cannot be conceived that their rebellious conduct is the result of volition, it becomes necessary, in seeking an explanation for it, to inquire into the conditions which might possibly account for their behavior.

Attention is at once attracted to the enormous vigor of the cancer-cell. No one who is familiar with the features of cancerous growths can fail to perceive that cancer-cells are endowed with a power which, in comparison with the normal cells, seems to be irresistible,

by virtue of which, not only are they able to crush local structures out of existence and thus destroy important functions, but also to appropriate to their own use a constantly increasing proportion of the nutritive supply which is necessary for the maintenance of the body as a whole.

The absence of resistance to invasion is not less remarkable than the vigor of cancer. The body is provided with a defensive and reparative mechanism, for the purpose of repelling the attack and repairing the injuries due to microbic and other foreign invaders, which it never fails to bring into action when the occasion arises. It is, therefore, of unusual significance to find that the body surrenders to the attack of cancer without an attempt at defence, and at first sight it might seem that its passive attitude was due to a loss of the power to resist, but further inquiry will show that this view is not correct. Proof of this is supplied by the fact that even when cancer is far developed, the defensive powers of the body are always aroused to action by the presence of pathogenic agents.

It appears, therefore, that while the body is capable of a vigorous defense against a foreign enemy, it is powerless to deal with one of its own species. Accordingly, it may be safely assumed, since the defensive mechanism is intact, that its absence of response is due to the fact that there is nothing in the nature of cancer to stimulate it into action. Parenthetically it may be added, that it is because of this want of specific bodily reaction that the cure of cancer is, and always will be, hopeless.

Physical and Metabolic Stimulation.—In considering the reasons for the growth of the cancer-cell, it is necessary to determine the extent to which physical and metabolic stimuli are influential in producing it. At the outset it is well to recognize that growth is really a multiplication of cells, and that the problem is, therefore, not directly concerned with the size or mass of a cancer, but with the conditions necessary for cell-division. At its origin every cancer is of microscopic size, and theoretically, even a single cell endowed with the power of unrestrained multiplication is a cancer: it is clear, therefore, that whatever the nature of the causative stimulus of cancer may be, its action is confined, at the beginning to a minute point, hence it is not only necessary to determine the nature of the causative force, but also the reason for its limited action.

The effect of physical stimulation upon the tissues is always to produce a greater or less degree of injury. Heat, light, electricity, dynamic force, or chemical action, are forms of energy necessary to the life-processes of all organisms, and every organism is adapted to them according to its nature; if, however, they are applied beyond the limits of adaptation—that is, to the degree of stimulation—their effects are always, in a strict sense, injurious. A certain degree of bodily heat, for example, is necessary for health, and within somewhat narrow limits the body is able to react normally to variations of external temperature. Any degree of heat beyond these limits causes a reaction which is pathologic, and which may vary from a slight hyperaemia to any degree

of severity consistent with life. The effects on the tissues of all other forms of physical stimulation are virtually similar; that is, their tendency is to impair or destroy, not to vitalize or construct—hence, on theoretical grounds it is contrary to reason to suppose that true growth of any kind, and especially such vigorous growth as cancer, can result from any form of stimulation which is essentially destructive in its effects. And there are no substantial facts of experience or experiment opposed to this conclusion. Doubtless it was natural to associate the evidences of stimulation or irritation present in precancerous lesions, with the causation of the disease, and it will later appear that there are good reasons for so doing. For the present, it is desirable to accentuate the fact that the lesions themselves are evidence of an action which is *degenerative,* not *regenerative,* in character.

It has been suggested that metabolic or nutritive disturbances are, in a manner not clearly defined, concerned in the causation of cancer, and it must be conceded that in so far as metabolism is capable of causing degenerative changes in the tissues, its relation to cancer is established: such a relation is, however, very remote, and its range is too limited to satisfy the conditions demanded by the facts of the disease. A broad view of cancer ranges over an enormous field, and takes in a great number of subjects, each of which in its proper perspective is indispensable to the picture as a whole: and just as it is impossible to form an adequate conception of a landscape by confining the view to a single object,

so it is impossible to understand cancer by concentrating attention upon a few of its features to the exclusion of the others.

To be of value, any theory of cancer must be able to include and coordinate *all its features* in a manner consistent with the well-ascertained facts of the disease and the principles of Science: failure in any cardinal respect is fatal to its acceptance. The facts of cancer are extraordinarily numerous and their relations extremely complex, and though from the view-point of investigation this is a disadvantage, in the opposite direction it is a fact of great value, for the reason that just as there can only be one pattern of key which will open a lock of intricate design, so there is only one theory which will coincide with all the facts of a complex problem: and just as ability to open the lock *proves* the accuracy of the key, so consistent and complete applicability to the facts, *proves* the truth of the theory. Many of the facts of cancer, and the relations between them, are established upon statistical material, the substantial accuracy of which is beyond question; others upon direct pathological observation; and still others by scientific inquiry and general knowledge: from all sources there is a large accumulation of more or less disconnected facts, the reliability of which is indisputable. For the present it is sufficient to gain an idea of their range, and this may be done most conveniently by grouping them as follows: (1) The relations of cancer to race, custom, habit, age, sex, occupation, civilized and primitive conditions. (2) Its geographical distribution. (3) Its

incidence on countries and localities. (4) Its incidence on parts and organs: selection of a preferred site: actual and relative immunity of certain parts. (5) Its tendency to progressive increase. (6) Its occurrence in animals. (7) Its clinical, pathological and biological characteristics. The relations of cancer, as indicated in the foregoing cannot be thoroughly understood without some knowledge of cancer statistics. A study of the enormous mass of details will give an idea of the immense field to be covered by any theory which purports to harmonize the facts of cancer in a manner consistent with a uniform principle of causation. Every fact must necessarily be directly, or indirectly, related to the cause of the disease, and, consequently, in the ultimate analysis, each fact rests upon a principle which is common to all, and can only be interpreted correctly when its relation to the whole is understood. A very superficial study is sufficient to show that metabolism, whether normal or abnormal, is totally inadequate to explain the phenomena of cancer. An attempt, for instance, to account for the variations in the mortality rates of cancer in countries, states or localities; or to find satisfactory reasons for the frequency with which certain organs are attacked, and the immunity relative or actual of others; or for the progressive increase of cancer, will demonstrate a complete absence of any connection between these matters and the phenomena of metabolism.

Clinical, pathological and biological considerations are in agreement with the view that metabolism is a process which *regulates the conditions of growth,* but it

is contrary to all our knowledge of life in general to suppose that it is capable of *causing growth.* It should not be forgotten that no tangible explanation has ever been given of the manner in which metabolism is supposed to act in the causation of cancer, and that the facts which have been suggested in support of it are entirely lacking in substance.

Disorders of metabolism are characterized by changes in the tissues, functions, or secretions, which are specific and peculiar to each disorder, whereas in cancer, while the general balance of metabolism may be disturbed owing to its increasing demand for nourishment, there is no specific change of any kind, all the functions continuing to act in a normal manner. Cancer appears to attack those who are overfed and those who are underfed in a fairly equal manner, and all classes of animals: herbivorous, carnivorous, or omnivorous. Starvation, or excess of food, appear to have no appreciable effect in accelerating or retarding the growth.

Superior vitality of Cancer-cells.—Growth is a vital phenomenon, and though an organism is dependent on nourishment and a suitable environment, its faculty to grow is determined by an inherent force conferred upon it from the beginning of its existence. Cancer cells are subject to the same conditions of nourishment and environment as the cells of the tissues in which they grow, and when it is considered that, notwithstanding the fact that the tissue-cells are most perfectly adapted to these conditions, cancer is able to invade them and thrive locally at their expense, and also at the expense of the

body as a whole, it will be realized that the *power* which determines such a superiority is the *essence of cancer;* and in seeking to understand the nature of the disease it is evident that no explanation of its phenomena can be complete which fails to account for such a pronounced characteristic.

It is significant that, with the exception of cancer, disease is never accompanied, either generally or locally, by any *true increase* of vitality, but on the contrary the tendency is towards debility and degeneration; hypertrophy of a part is the result of reaction to stimulation, or changes in environmental or nutritive conditions, but is never due to a local increase of vital force, and in this respect differs fundamentally from cancer.

It has been said that "The cancer-cell is immortal," and though this cannot be literally true, it serves to emphasize the enormous vitality which cancer-cells possess. Experimental evidence of this is supplied by the fact, that the same strain of cancer has been continued by transplantation through a long, unbroken series, with no apparent loss of vigor.

Cancerous growths are homologous with normal tissues.—The tissues of the body are of a quality and nature peculiar and special to each individual, and every substance from a source outside the body itself is "foreign" and unacceptable to them. The presence of a foreign substance in the body is followed by a reaction which results in its destruction or elimination. The degree of reaction varies according to the nature of the

foreign material; for instance, blood from an animal of a widely-differing species causes a well-marked reaction and is rapidly destroyed, while blood from an animal of the same species produces only a slight reaction and is slowly eliminated. In order, therefore, to be tolerated in the body, a substance must be *homologous;* that is, of the same quality and nature as the tissues, and it would appear that a substance which is homologous with the tissues of one individual, is foreign to, or heterlogous to, any other.

A reaction is, therefore, an index by which it is possible to estimate certain subtle differences in the nature of a substance as compared with the tissues of an individual. We may be absolutely sure that if a cancerous growth were the result of microbic, parasitic, or other foreign agency, that the reactive forces of the body would be aroused to oppose it. But we find that this never occurs. In the presence of a cancerous growth, the body generally, and the tissues locally, remain entirely passive; not because they have lost the power to resist, but because there is nothing in the nature of a cancerous growth to stimulate reaction. Consequently, it may be definitely concluded that cancerous growths are homologous with the tissues and are accepted by them in the same manner as a normal part.

The course of a cancerous growth is usually terminated by the death of its host, owing to impairment of important functions, hæmorrhage, or septic poisoning, following necrosis or ulceration—but it is evident that such events are, in a broad sense, accidental, and are

not due to any inherent quality or influence of the growth itself. If a cancerous tumor were imagined growing to an unlimited size, in a part where it did not interfere with the function of any organ, and without necrosis, ulceration, or other pathological change, it would grow in a similar manner, but differing in degree, to corresponding normal tissue. There would be no reaction, and the body would remain in good health, and except for the bulk of the growth would suffer no inconvenience. As its size increased, however, a point would be reached where, on account of its increasing demand for nourishment, the balance of nutrition would be disturbed, after which debility, emaciation and death would follow in due course. Theoretically, therefore, cancer is injurious only because its growth is out of proportion to the general economy of the body, not by reason of any *active* influence. Cancer has no specific action, and therefore causes no symptoms: in the early stages it gives rise to no apparent effects; at a later period they are determined only by its size and situation.

The homologous nature of cancer-cells points very definitely to the fact that they take their origin from normal tissue cells, and if further evidence of this were required, it could be supplied by a study of the various types of the disease; it is inconceivable that foreign cells implanted in the tissues could exhibit the variety of type which is found in cancer, and that the type of each foreign cell should always be morphologically identical with the cells of the tissues in which it happens to fall.

Cancer, then, must be conceived of as a growth composed of cells which are the offspring of, and therefore biologically identical with, normal cells, but differing from them in one respect only, namely, the possession of greatly increased vital power, by virtue of which they are able to outgrow the normal cells and suppress them. The problem, therefore, resolves itself into the question of the manner by which those normal cells at the point of origin of cancer, became endowed with such increase of vital power.

Fertilization of normal cells.—If physical or metabolic stimuli cannot supply the form of energy required, there remains only one other possibility to which cancer can be attributed, that is, vital stimulation or fertilization. A very superficial view of the effects of fertilization is sufficient to convince us that the forces generated by it are capable of causing the phenomena of cancer, and deeper reflection will render it equally convincing that it is *the only form of stimulation to which, not only cancerous growth, but also all other forms of growth, can be attributed.*

A tissue-cell in the body of a highly-organized animal is adapted for a special function, and is not required to reproduce itself beyond the limits determined by the hereditary characters of the body as a whole. But it cannot be assumed, because its reproductive power is thus limited, that the faculty of independent reproduction for the propagation of its species, which is a universal result of fertilization in living organisms, has ceased to exist. A tissue-cell is a biological entity, and

theoretically *must possess all the fundamental faculties of living matter.* On this ground alone, and more especially since proof to the contrary is entirely wanting, there is sufficient reason to assume that tissue-cells possess the faculty of independent reproduction under appropriate stimulation.

It should be remembered that, normally, no opportunity for the union of a fertilizing element with the nucleus of a tissue-cell can occur owing to the effective barrier presented by the intact surfaces of the body. It is probable also, for reasons of a very obstruse kind, that nuclear union between organisms of different species is not commonly possible, consequently it is not to be supposed, even though free access of a fertilizing element to a tissue-cell were permitted, that reproductive stimulation would follow in every case.

Observation has rendered it abundantly clear that fertilization never occurs between organisms of widely different species, as, for instance, to state extreme cases, between plants and animals, or between insects, birds, fishes or mammals. Among closely-related organisms, however, fertilization is possible within limits which appear to be determined by the degree to which they are differentiated from each other, not only as regards their morphological character, but more especially with respect to those specific qualities which are peculiar to their nature. There are inherent qualities, too subtle for analysis, in the nature of every species, which are derived from its ancestry, and transmitted by fertilization to succeeding generations. In cases where two or

more species spring, not too remotely, from the same ancestral stock, they may possess, in greater or less degree, these hereditary qualities in common, and it would appear that it is only under such a condition that fertilization between them is possible. There are doubtless many factors, beyond the range of investigation, which require to be understood before our knowledge of the principles underlying fertilization is complete. Only the broadest facts of observation and experiment are at present available, but on the basis of these it seems safe to assume that the possibility of fertilization between organisms of different species depends largely upon the *degree of their relationship to a common ancestor, and a similarity of hereditary characteristics.*

The theory of evolution postulates an organism of the simplest type as the common ancestor of all living things. Such an organism can only be conceived of as a protoplasmic body possessing the essential faculties of reproduction, growth, and metabolism, but without functional or morphological differentiation. It must be assumed that some have male, others female potency, but that, for the reason that no differentiation has occurred, the sexes are indistinguishable from each other, and also that fertilization takes place between them, not for the transmission of hereditary characters, since there are none to transmit, but for the purpose of rejuvenation only.

From such a theoretically simple organism it is conceivable that differentiation might occur in several directions, and thus originate several types of simple or-

ganisms, each distinct from the others, and from the common ancestor. Functional characters, usually accompanied by corresponding morphological differentiation, make their appearance, by virtue of which each organism is enabled to react to the environmental condition differently to the others in some particular. Such changes of function and structure become fixed characteristics, and are renewed and transmitted by fertilization to succeeding generations.

Organisms thus differentiated in the first degree are raised to a higher grade in the scale of evolution, but they are still closely related to their common ancestor and to each other, and since the range of their characteristics is very limited, a considerable proportion of their nature must still be common to all. For these reasons it is to be expected that fertilization between such different species in the lowest ranks of evolution should occur with much greater freedom than in those which have reached a higher degree of complexity. It would, in fact, seem that there is an inverse relation between organization and fertilization: a low degree of organization tending to favor fertilization; a high degree tending to limit it.

It is interesting to find that the results of experimental research are in agreement with the foregoing. Discussing hetorogeneous hybridization, Dr. Jacques Loeb, in his very illuminating work "The Mechanistic Conception of Life", says:*

*Page 196, "The Mechanistic Conception of Life." Biological Essays by Dr. Jacques Loeb, M. D., Ph. D., Sc. D. The University of Chicago Press, Chicago, Illinois.

"It was held until recently that hybridization was not possible except between closely related species, and that even among these a successful hybridization cannot always be counted upon. This view was well supported by experience. It is, for instance, well known that the majority of marine animals lay their unfertilized eggs in the ocean and that the males shed their sperm also into the sea-water. The numerical excess of the spermatozoa over the ova in the sea-water is the only guarantee that the eggs are fertilized, for the spermatozoa are carried to the eggs by chance and are not attracted by the latter. This statement is the result of numerous experiments by various authors, and is contrary to common belief. As a rule all or the majority of individuals of a species in a given region spawn on the same day, and when this occurs the sea-water constitutes a veritable suspension of sperm. It has recently been shown by experiment that in fresh sea-water the sperm may live and retain its fertilizing power for several days. It is thus unavoidable that at certain periods more than one kind of spermatozoa is suspended in the sea-water and it is a matter of surprise that the most heterogeneous hybridizations do not constantly occur. The reason for this becomes obvious when we bring together mature eggs and equally mature and active sperm of different families. When this is done no egg is, as a rule, fertilized. The eggs of a sea-urchin can be fertilized by sperm of their own species, or, though in smaller numbers, by the sperm of other species of sea-urchins, but not by the sperm of other groups of echinoderms, *e. g.*,

star-fish, brittle-stars, holothurians, or crinoids, and still less by the sperm of more distant groups of animals. The consensus of opinion seemed to be that the spermatozoon must enter the egg through a narrow opening or canal, the so-called micropyle, and the micropyle allowed only the spermatozoa of the same or of a closely related species to enter the egg.

"It seemed to the writer that the cause of this limitation of hybridization might be of another kind and that by a change in the constitution of the sea-water it might be possible to bring about heterogeneous hybridizations, which in normal sea-water are impossible. This assumption proved correct. Sea-water has a faintly alkaline reaction (in terms of the physical chemist its concentration of hydroxyl ions is about 10^{-6}n at Pacific Grove, California, and about 10^{-5}n at Woods Hole, Massachusetts). If we slightly raise the alkalinity of the sea-water by adding to it a small but definite quantity of sodium hydroxide or some other alkali, the eggs of the sea-urchin can be fertilized with the sperm of widely different groups of animals. In 1903 it was shown that if we add from about 0.5 to 0.8 c. c. n/10 sodium hydroxide to 50 c. c. of sea-water, the eggs of *Strongylocentrotus purpuratus* (a sea-urchin which is found on the coast of California) can be fertilized in large quantities by the sperm of various kinds of star-fish, brittle-stars, and holothurians; while in normal sea-water or with less sodium hydroxide not a single egg of the same female could be fertilized with the star-fish sperm which proved effective in the hyperalkaline sea-water. The

sperm of the various forms of star-fish was not equally effective for these hybridizations; the sperm of Asterias ochracea and A. capitata gave the best results, since it was possible to fertilize from 50 per cent. to 100 per cent. of the sea-urchins' eggs, while the sperm of Pycnopodia and Asterina fertilized only 10 or 2 per cent. respectively of the same eggs.

"Godlewski used the same method for the hybridization of the sea-urchin eggs with the sperm of a crinoid (Antedon rosacea). Kupelwieser afterward obtained results which seemed to indicate the possibility of fertilizing the eggs of Strongylocentrotus with the sperm of a mollusk (Mythilus). Recently the writer succeeded in fertilizing the eggs of Strongylocentrotus franciscanus with the sperm of mollusk—Chlorostoma. This result could only be obtained in sea-water the alkalinity of which had been increased (through the addition of 0.8 c. c. n/10 sodium hydrozide to 50 c. c. of sea-water). We thus see that by increasing the alkalinity of the sea-water it is possible to effect heterogeneous hybridizations which are at present impossible in the natural environment of these animals.

"It is, however, conceivable that in former periods of the earth's history such heterogeneous hybridizations were possible.

". . . . .So far as the question of heredity is concerned, all the experiments on hetrogeneous hybridization of the egg of the sea-urchin with the sperm of star-fish, brittle-stars, crinoids, and mollusks have led to the same result, namely, that the larvae have *purely maternal char-*

acteristics and differ in no way from the pure breed of the form from which the egg is taken.

"..... It might be argued that in the case of heterogeneous hybridization the sperm nucleus does not fuse with the egg nucleus, and that, therefore, the spermatozoon cannot transmit its hereditary substances to the larvae. But these objections are refuted by Godlewski's experiments, in which he showed definitely that if the egg of the sea-urchin is fertilized with the sperm of a crinoid the fusion of the egg nucleus and sperm nucleus takes place in the normal way."

It is too firmly established to be seriously disputed that hybridization among species of high rank cannot occur except within extremely narrow limits. Dr. Loeb's work therefore shows very definitely that fertilization between species of the rank of sea-urchins is possible over a much wider area than among species of a higher type, and so establishes a basis of concrete facts for the assumption that the possibilities of fertilization are limited directly in proportion to the degree of differentiation to which an organism has attained. Hence, among organisms of the lowest ranks, it is to be expected that the limitations to the occurrence of hybridization should be of the broadest kind.

The foregoing principle applied to cancer is of great theoretical importance. Cancer only arises in epithelial, glandular and connective tissues, and, probably, white blood-cells, all of which, when considered as independent biological entities, may be classed as belonging to the same rank of evolution as protozoal organisms. The clear-

est illustration of this is found in the resemblance between the white blood-cells and the Amœba, but the reasons which are valid for classifying them together also apply equally to the other cells, if their functional modifications are taken into consideration and due allowance made for them.

Cancer, therefore, arises from cells which in the abstract are biologically independent organisms similar to an Amœba, hence, for reasons already discussed, fertilization between them and species of organisms of low rank may be expected to occur very readily.

The cell-nucleus.—The essential fact of fertilization is the union of two cell-nuclei; one having male, the other female, potency or polarity. The most striking result of the process is the generation of vital energy, by which the female cell is quickened into reproductive activity, which continues until the individual thus created is mature.

It is impossible to fully conceive the nature of fertilization; there is, however, a certain resemblance between it and chemical union, which may be advantageously considered. In a chemical process, elementary atoms having dissimilar affinities unite, with a generation of energy, to produce a substance, different from, yet possessing certain latent qualities derived from the atoms which combined to create it. Similarly, in fertilization protoplasmic elements having dissimilar affinities unite, with the generation of vital energy, to produce an individual differing from (but in a more refined manner),

yet inheriting, the characteristics of each protoplasmic element from which it was formed. Theoretically it is possible that vital energy and chemical energy are forms of the same force, and that the differences between vital and chemical manifestations are due, not to the form of energy, but to the nature of the substance upon which it acts. The molecular constitution of any chemical substance is relatively very simple, and never varies, but protoplasm is so infinitely complex that it is doubtful whether the same chemical constitution and molecular structure has ever existed more than once. Some idea of these complexities may be gained when it is remembered that, among infinite numbers, the crystalline design of any snowflake has never been repeated, though the symmetry of each is so perfect that the operation of a uniform principle in their formation must be admitted. If, then, such variation is possible in a simple substance such as water, it is conceivable that in a substance with the complex structure of protoplasm the possible number of variations would be so much greater as to make the others appear insignificant.

It might be supposed that the chemical constitution and structure of protoplasmic molecules are arranged according to a design which is different for each species, and simple or intricate in proportion to their degree of organization. In order that fertilization should occur between two cells it would be necessary that the protoplasmic molecules of each should possess all the characters pertaining to the protoplasm of the species; or, in other words, the male and female protoplasmic mole-

cules must be exact counterparts with respect to a specific design.

Within species there are varieties: hence, it may be further supposed that additional features, special for each variety, are imposed upon the basic design of the species. For fertilization to occur it is not necessary that the protoplasmic molecules of both the male and female cells should possess all of such secondary characteristics; if, however, the characters of the male differ from those of the female the offspring will be of a hybrid type.

A greater degree of intricacy in the design is reached by the addition of those characteristics which are peculiar to families, and a still greater and final by those which are confined exclusively to the individual.

The characters referred to in the foregoing are derived from the ancestry of an individual, and are transmissible to succeeding generations, and it is upon the cell-nucleus that the responsibility for their preservation and transmission rests. Professor Hugo de Vries, in his admirable work* "Intracellular Pangenesis" says: "The first author who described the nucleus as the organ of heredity was Ernst Haeckel. In the second of his 'Generelle Morphologic der Organismen' he established this conception, founding it especially on the behavior of the nucleus during cell-division. For him the inner nucleus has the work of transmitting the hereditary characters, the outer plasma has the part of adapta-

*"Intracellular Pangenesis," Hugo de Vries. Open Court Publishing Co., Chicago, Illinois.

tion, accommodation, or adjustment, to the conditions of the outer world. And just as the nucleus plays its principal role in propagation, so is nutrition the chief task of the plasma. In the lowest non-nucleated organisms the two functions are not yet separated.''

Potentially, the characteristics of every type of cell in the body are concentrated in the molecules of the protoplasm, (or more precisely the nucleoplasm) of the reproductive cells; and it would seem as though fertilization were the commencement of a process of unfolding or distribution, in which each type of cell receives those characters which are appropriate to its function, and which, in leucocytes, epithelial, glandular, connective-tissue, and other cells, are not more numerous or complex than those of a protozoal organism. The reproductive cells reproduce the entire animal: all other cells, if they divide at all only reproduce cells similar to themselves, and in this, as in all other fundamental respects, agree with free unicellular organisms.

The general resemblance, which has been commonly observed, between cancer-cells and embryonic-cells, is doubtless due to the fact that both possess enormous vitality, and are rapidly-growing. There is also a particular resemblance between them concerning the manner of division of the cell-nuclei, which in each case is by mitosis. The meaning of mitosis is not fully understood, but it seems to be generally agreed that it is a process whereby, in cell-division, the hereditary substances present in the nucleus may be equally distributed. If this interpretation is correct, the value of mitotic di-

vision as an evidence of fertilization becomes considerable, and, applied to the cancer-cell, of great importance in corroborating or contradicting any conclusions concerning its nature. Further inquiry is necessary, but for the present it is sufficient to observe that the facts of cell-division in cancer are in agreement with the theory that fertilization is the principal factor in its causation.

There is an interesting point, apparently unnoticed hitherto, concerning the behavior of cell-nuclei in wounds, which has some relation to the causation of cancer. It has already been stated that a lesion of the body-surfaces is an essential factor in the causation of cancer. It so happens, that, solely as a matter of scientific interest, somewhat elaborate observations have been been made on the behavior of cell-nuclei in wounds and other conditions of irritation, which are of value in relation to cancer. In his work previously referred to Professor Hugo de Vries* says: "Tangl observed bulb-scales of Allium Cepa, which had been recently wounded for example the day before. He saw that near the wound-surface the nuclei are not, as otherwise, irregularly distributed over the cells, but that they had gone to that side of their cells which was nearest to the wound. With them the granular plasm was also accumulated on those walls. The shorter the distance from the wound, the more pronounced was the phenomenon, but as far away as about 0.5 min. it could still be distinctly seen.

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*"Intracellular Pangenesis," Hugo de Vries, Open Court Publishing Co., Chicago, Ill.

These conditions probably indicate that the process of regeneration which the wounds usually cause, proceed here under the influence of the nuclei.

"Haberlandt studied the position of the nucleus during the process in a great number of cases in which the cells of the higher plants show a more vigorous local growth in some definite part of their circumferences. He did so partly where, through localized surface growth, the shape of the cells change; partly where unnatural thickenings of the membranes or a definite wall-sculpture are started. And although, owing to the abundance of individual phenomena, a rule without exceptions could not be expected, he found, on the whole, that the nucleus most frequently turns to where the growth is strongest, and remains longest where the latter continues longest.

"According to Korshelt, the same rule is valid, in a general way, for the animal cell. With chiefly unilateral or local activity of the cells, this investigator succeeded, in a number of cases, in observing for the nucleus a definite position which was as near as possible to the place where this process was going on."

These very interesting observations tend to support the view that a tissue-cell is a sensitive organism, and that through impressions received by the nucleus it reacts in an independent manner to changes in the conditions of its environment. Their importance with respect to cancer, however, lies in the fact that, in a lesion, the nucleus approaches as near as possible to the sur-

face, in which position it is most easily accessible to a fertilizing agent.

Cancer only originates in female cells.—The view that cancer is the result of fertilization implies the co-operation of the two sexes, and it is therefore theoretically important to consider independently the question of the sexual nature of the tissue-cells. At the outset, it should be recognized that the ultimate nature of sex is one of the most difficult problems conceivable. Fortunately it is not necessary for the present purpose to enter upon a discussion of many abstruse questions which a full inquiry into the subject would demand, but it may be said that there are no established facts or reasons to oppose the view that, independently of the body as a whole, tissue-cells have a sexual nature. For example, an animal is male or female by virtue of its reproductive organs, but the sexual character of the animal as a whole does not determine the nature of the tissue-cells. Epithelial, glandular, nerve-cells, and so forth, in a male animal, do not differ from those in a female, consequently, whatever the sexual nature of any type of cell may be in the one case, it will be the same in the other; in other words, the sexual character of tissue-cells is independent of the sex of the animal to which they belong.

In order to classify tissue-cells as male or female, it is sufficient for the present purpose to determine whether or not they possess the faculty of division. Only female cells have the power to divide: male cells always remain single. Therefore, cells which divide are female, and

conversely those which never divide are male. Nerve-cells are the best example of those which always remain single, and it is extremely significant that *these cells are never found in cancer, or any other form of new-growth.* The same is probably also true of striped muscle-cells.

Now, fertilization of male cells is obviously a biological impossibility, and on the basis that, for the reasons given, nerve-cells and probably muscle-cells are of male nature—and also, that cancer and other new-growths are the result of fertilization—it is clear that *male cells are excluded from an active part in the formation of new-growths.* On the negative side, therefore, the facts concerning the relation of nerve-cells, muscle-cells, and doubtless others of the same nature, to cancer and other neoplasms, are in perfect harmony with the theory suggested.

Concerning those tissue-cells which are theoretically of female nature, there is much more to be said. On reference to the extract from Dr. Loeb's work, already given, it will be found that when an ovum is fertilized by the sperm of an animal of a foreign species, *the resulting embryo is always of the maternal type.* Further, Dr. Loeb and others, by physical stimuli applied to ova of various species, have succeeded in exciting reproductive activity in them, and in this manner have raised fully developed embryos: in these cases, also, the embryos have invariably been of the maternal type. Two conclusions, of great importance with respect to cancer, may be derived from these experiments: firstly, that *reproduction is the exclusive faculty of female cells*:

and secondly, that *no cell can reproduce other than its own type; or, in other words, every cell must "breed true."*

Another kind of evidence, pointing in the same direction, is supplied by the following extracts from the work of Professor de Vries, previously referred to, dealing with the subject of "Fertilization in Cryptogams," he says: "Schmitz in his important monograph on the chromatophors of the algae has comprehensively demonstrated that these structures which, at each vegetative cell-division, are transmitted from the mother cell to its daughter cells, are usually entirely lacking in spermatozoids. The egg-cells, however, always possess these organs. After fertilization they multiply by division, and thus form the chromatophors of the new individual. In regard to this point the organization of the protoplasts is therefore inherited directly from the mother and not from the father." Further on, he continues: "This comparative study bridges the chasm lying between conjugation and fertilization, which is no doubt chiefly due to the fact that, in the latter the organization of the protoplasts is inherited morphologically from the mother only, while in the former, in some cells, the inheritance is from the mother, in others from the father."

The foregoing considerations are sufficient to justify the view that the cells of the tissues and organs of the body possess male or female qualities which are independent of the sex of the animal to which they belong. It may now be pointed out that the fact that cancer and other new-growths always originate in those cells which

by theory are female, and never in cells which theoretically are male, is not only of great value as a corroboration of the conclusions derived from a very wide field of inquiry, but also because the reasons which serve to explain it are consistent, in a very special manner, with the conditions which the theory of fertilization demands.

Analogy between ovum and pathological cells.— It is very interesting to find that, more than half a century ago, Virchow, the "Father of Modern Pathology," pointed out not only the resemblance between reproductive growth and pathological new-formations, but also recognized that in each case the nature of the causative stimulus was identical. Discussing, in the work already referred to, the "Nature of Formative Stimulation (Artificial Parthenogenesis)," Dr. Jacques Loeb says: "The title of this paper was chosen in reference to Virchow's paper on 'Stimulation and Irritability' (Virchow's Archiv. XIV. 1, 1859) in which he discriminates between the forms of stimulation: functional, nutritive and formative. By formative stimuli he means those which give rise to nuclear and cellular division. He considers as the classic example for formative stimulation the fertilization of the egg, and the parallel drawn by him between this process and the causation of a pathological process of growth is so characteristic that we may quote it in full:

" 'If we admit the identity between the pathological and the embryonic neoformation, the egg will have to be considered as the analogue of the pathological mother-cell and the act of impregnation as the analogue of path-

ological stimulation. This view is not essentially altered through the discovery of the entrance of the spermatozoon into the egg, since there is no reason to consider the spermatozoon as the direct morphological starting-point for the development of definite parts of the egg. If, as seems to be the case, the spermatozoa are dissolved in the egg, they carry into it only certain chemical substances, which serve as specific stimuli, by calling forth new chemical and morphological arrangements of the atoms. Each specific contagium offers the same possibilities.'

"The supposition prevalent at Virchow's time, that the spermatozoon is entirely dissolved in the egg was not correct; but his view, that the spermatozoon carries chemical substances into the egg, which form the stimulus for its development, is perfectly correct; and likewise the analogy between the the causation of the development of the egg by a spermatozoon and the causation of a pathological growth seems correct."

The meaning of the foregoing passage is too unmistakable to allow of a doubt that Virchow clearly realized the nature of pathological new-growths, and of fertilization as an underlying principle in the causation of pathological phenomena. His famous phrase, "Omnis cellula e cellula," has been accepted as an ultimate truth upon which every pathological development must directly or indirectly rest, but there is no pathological phenomenon to which it may be applied so literally or so closely as to cancer and other new-growths. The perfect manner in which the theory of fertilization harmon-

izes with the established facts of new-growths is, apart from every other consideration, sufficient to justify a presumption of the strongest kind in favor of a causative relation between them. Nothing in the whole range of Science is more rigidly true than the fact that every organism must conform to its hereditary type, and there is no room to doubt that cancer and other new-growths agree, in this respect, with other living things: consequently, we are compelled to recognize, not only that new-growths are the offspring of the cells of the tissue in which they originate, but also, that like all other offspring they are the result of formative stimulation or fertilization.

Cancer and other new-growths are hybrids.—It has already been pointed out that tissue-cells must be considered as belonging to the lower biological ranks, and also that fertilization can only occur among organisms which do not differ very widely in the nature or degree of their organization. The causative agent of cancer must, therefore, spring from a lowly-developed organism which necessarily is of a foreign species. Consequently, cancerous and other new-growths consist of cells which are hybrid.

It should be realized that at the moment of the union of a male with a female cell, both cells theoretically cease to exist, and in their place a *new individual appears which proceeds to develop independently according to its hereditary nature.* Every individual thus created coincides with the maternal type, but since it is a combination of maternal and paternal qualities, its

nature must necessarily differ in certain subtle respects from either, and in cases of heterogeneous union it is reasonable to suppose that such differences would tend to be wider.

Let it now be supposed that a tissue-cell has been fertilized by the male element of a foreign species of organism. Theoretically the tissue-cell has then gone out of existence, and in its place an organism has appeared which morphologically is indistinguishable from it, but which is endowed with independent vital powers of a somewhat different kind.

Such an organism conforms to the maternal type, and from this viewpoint may be considered to be in the environment which is natural to its species. It is abundantly supplied with appropriate nourishment and by virtue of its situation in the body of its host it is protected from all deleterious influences. The conditions under which it exists are therefore those which are suitable in the fullest degree to its development.

For two reasons this newly-created organism possesses vital powers which are enormously superior to the cells of the tissues. Firstly, the tissue-cells are tending to lose vigor on account of age, while the new organism, being at the commencement of its career, is at the point of its maximum potency; secondly, because the vital energy of any tissue-cell is not derived from an independent fertilization, but from the store which is common to all the cells of the body, and which is distributed, not with a view to the highest development of any cell, but according to the requirements of the body as a

whole. A single tissue-cell, therefore, receives only a minute proportion of the total vital energy of the body, whereas the organism created by direct fertilization possesses the whole of the energy generated in the process. As generations of daughter-cells arise, each receives its due proportion of the original energy, but as their numbers continue to increase it is evident that a point must ultimately arrive at which the supply is exhausted: growth would then cease, and sooner or later the existing development would die and disappear. But this event seldom or never occurs within the lifetime of the host.

For the foregoing reasons, there is always an enormous difference of vital power between the tissue-cells of the body and any colony of cells which result from fertilization in the manner suggested, with the balance on the side of the latter; hence, it is not surprising that the growth of such a colony should be "riotous", irregular, or excessive. Apart, however, from the influence of its superior vitality, it is to be expected that the growth of such a colony should be out of conformity with the design of the body, by reason of the fact that it develops according to its own nature which, it has already been stated, is independent, and different from the cells of the tissues of its host.

Owing to change resulting from fertilization in the constitution of the protoplasmic molecule, it cannot be considered that the fertilized organism and its progeny are strictly homologous with the tissues in which they originate. There is, however, the same relation between

them as that which exists between an embryo and its maternal tissues, and hence it may be presumed that no closer approach to identity of nature is theoretically possible; and just as there is no vital reaction in the latter case, so, for the same reasons, none is to be expected in the former.

General remarks.—The question of fertilization of a tissue-cell, in connection with cancer and other new-growths, does not appear hitherto to have been seriously considered; but it cannot be doubted by those who are familiar with these diseases that the stimulus of fertilization is not only capable of causing them, but that it is the only form of stimulation which is able consistently to explain their manifestations in general, and the relations between the various types of the disease and the tissues of the body in particular. In endeavoring to find valid objections to this theory, it has not been possible to discover any of sufficient weight to counterbalance the force of the considerations discussed. Perhaps the absence of authoritative support is the strongest objection that can be raised; but it is unsubstantial, for the reason that sufficient advance in biological or pathological science has not yet been made to render any authority in such matters absolute; and it seems proper to point out, that if it were necessary that every departure from existing views should receive the sanction of authority before becoming eligible for consideration, progress would be impossible.

It may be said that the theory suggested does not introduce any new principle, but is an extension of the

principle which is recognized as the foundation of all vital phenomena. The central point in the matter is the application of the principle of fertilization to tissue-cells, and if the reasons which have been given, for the purpose of establishing the possibility of such application, are valid, a distinct advance toward the solution of the "Cancer Problem" will have been gained.

PART II

Thus far only theoretical matters have been considered, but there is a practical side to the subject, from which not only complete corroboration of the foregoing conclusions may be obtained, but also a clear indication of the means by which cancer may be prevented.

This practical side of the subject deals with facts entirely remote from those already discussed, and which are so numerous and diverse that without a correct clue to their meaning, it is impossible to distinguish any relation between them. There is, for instance, no apparent connection between the facts of cancer with respect to (to mention only a few of the most general): Age, sex, locality, race, habit, custom, occupation, social station, civilization, progressive increase, geographical distribution, and incidence on parts and organs of the body. These, and a large number of other facts, are the features by which the character of cancer is to be recognized, but at present they are in such a state of disarrangement that their meaning is unintelligible. Now, any theory which is able to coordinate facts of such number and diversity, to form a consistent and intelligible whole, must, by virtue of such a faculty, be correct. This may be illustrated by the manner in which diverse rays of light in passing through a lens are converged to form an image. To form an image it is necessary that the lens should consist of appropriate material without flaws, and that its form should be uniform and perfect. The image will be clear and its detail in proper propor-

tion, or vague and distorted, according as the lens is perfect or otherwise. A perfect image implies a perfect lens, and vice versa, or, in other words, the relation between a lens and its image is so exact and constant that it has the value of proof. Similarly, the degree to which the facts of cancer can be consistently coordinated, is a proof of the degree to which the theory applied to them is correct. It is, therefore, now proposed to examine the features of cancer, through the medium of the theory of fertilization, in order to determine their meaning with respect to each other and to the whole.

Cancer is a universal affection, distributed throughout the world, not only in human beings, but also, there are good reasons to believe, among all animals, including fishes. It does not, however, occur everywhere equally, but is extremely irregular both with respect to individual countries and particular localities of the same country. The following figures, from Dr. Frederick L. Hoffman's elaborate work,* "The Mortality from Cancer Throughout the World," will give a general idea of the extent of its distribution, and of the variations in its incidence. The death-rates from cancer during the period 1908-1912, per 100,000 of population, were in the following countries and cities:

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*"The Mortality from Cancer Throughout the World," Frederick L. Hoffman, LLD. etc. The Prudential Press, Newark, New Jersey.

Countries.		*Cities.*	
Switzerland	124.3	Copenhagen	161.3
Holland	106.4	Berlin	133.5
England and Wales.	97.6	Amsterdam	116.7
Germany	87.1	London	111.7
New Zealand	75.2	Budapest	102.6
U. S. Registrative Area	74.7	Sydney	90.1
Uruguay	66.6	Moscow	94.8
Japan	64.3	New York	77.1
Hungary	45.5	Tokio	73.6
Hawaii	40.7	Constantinople	34.8
Chile	35.6	Calcutta	11.7

Distribution of Cancer universal, with irregular incidence.—These figures are sufficient to show that the cause of cancer exists universally, and that it prevails in varying degrees according to locality. Now, the variations in the incidence of the disease must be due, either to certain local predisposing influence, or to the presence locally of the causative agent in greater abundance, or to both. The large number of predisposing conditions which in some degree determine its incidence, is one of the most remarkable features of cancer, and by reason of its diverse relations, one of the most valuable. Modern opinion justifiably attaches considerable importance to the causative effects of certain influences, such as: tobacco-smoking, betel-chewing, tar, paraffin, soot, X-rays, warts, moles, ulceration, long-continued irritation or inflammation, etc.; all of which, and many others, it will appear later, are possible *factors, or modifying influences,* but are totally inoperative as *ac-*

tive causes of the disease. Their value lies in the fact that each must be related to the cause of disease, not necessarily in the same manner, but in a way which is consistent with a principle common to all.

We have reached the conclusion that cancer is a universal disease, and that its cause is a fertilizing agent; it is, therefore, evident that, since such an agent must exist in some medium, both the agent itself and the medium in which it exists are also universally distributed. Also, cancer attacks all vertebrate animals, including fishes, hence its causative agent must exist in a medium which is common to terrestrial and aquatic animals; and of such media there are only three in which a fertilizing agent could develop or exist, namely: organic matter, mineral or earthy matter, and water.

Now, water which has reached the surface of the ground, and as used for ordinary purposes, is, unless artificially treated, always contaminated with organic and earthy impurities, which in association with light, air, temperature, etc., supply the conditions necessary for the various living organisms which are never absent from the waters of rivers, streams, lakes, pounds and reservoirs.

It is sufficient, for the present, to note that water is a medium common to fish and other vertebrates, and also that it is of universal distribution, and suitable for the development and existence within it of a fertilizing agent; it is necessary, now, to demonstrate that water is *the only medium,* on the basis of the theory of fertilization, which is *consistent with the facts of cancer.*

The incidence of cancer on parts and organs of the body is in direct relation to their association with water. —Cancer has a tendency to select for attack certain parts and organs, but with regard to this a distinction must be made between Carcinoma and Sarcoma. Carcinoma shows a marked predilection for the stomach, uterus, breast, and skin, and seems to avoid some organs, as the lungs, brain, and kidneys, almost entirely. Sarcoma shows no tendency to select any part, and appears fairly frequently in organs where Carcinoma is found extremely seldom. In attempting to explain this difference it is not to be supposed that Carcinoma possesses any inherent power of selection, but rather that the place in which it develops is already prepared for it by those preexisting or "precancerous" affections to which certain situations are well known to be liable. Also, the manner in which Carcinoma spreads seems to indicate that it does not enter the blood stream, but is confined to the lymphatic circulation, and so has no great tendency to be carried far from its point of origin. On the other hand Sarcoma does not depend upon a preexisting condition of the tissues, but in all probability upon injury, and accordingly its situation is largely a matter of chance. Its causative agent probably enters the blood-stream and is carried by it to any part of the body indifferently. There is no reason to doubt that Carcinoma and Sarcoma are due to the same cause, or that there is any fundamental difference between them. Carcinoma develops from cells of epiblastic and hypoblastic origin, Sarcoma from cells of meso-

blastic origin; and the frequency with which any part of the body is attacked is in proportion to the degree to which the cells of these tissues are exposed to the invasion of the causative agent. If the protective surfaces of the body are perfect, the development of cancer in any form is impossible, even though the causative agent be present.

The following figures from the mortality returns for the year 1913, in the Fourteenth Annual Report of the Census Bureau, will show the proportion in which the disease occurs in the various organs of the body:

General rate	78.9
Buccal Cavity	3.1
Stomach, Liver	31.2
Peritoneum, Intestine, Rectum	10.5
Female Genital Organs	12.2
Breast	7.3
Skin	2.7
Not specified	11.9

It is very significant that, notwithstanding every part of the body is liable to the attack of cancer, only nine parts are specified in the foregoing table, and that these comprise approximately 85 per cent. of all cases of the disease; but it becomes still more significant, when it is realized that not only is the incidence of cancer confined to a few organs, but that its attack is directed to a comparatively small area in each, as, for instance, in the stomach to the pylorus; in the uterus to the cervix; and in the skin to the hands and face.

Cancer-incidence, then, is limited to areas which, compared with the whole body, are few in number and small in size, but the experience of many years has clearly shown that these particular areas are the favorite sites of certain affections which, for the present purpose may be considered as lesions, and which have been observed to precede almost invariably the appearance of cancer. From these facts it seems reasonable to suppose, and in view of other evidence it cannot be doubted, that *cancer appears in situations where the surface-coverings of the tissues, by reason of the presence of a lesion, are defective.*

Hence, cancer is strictly a local disease, and is determined with respect to one factor in its causation, by the condition of the surface of the tissues at its place of origin. Now, a lesion may vary from a superficial microscopic defect, exposing a few living epithelial cells, to a breach of a wide surface and sufficient to expose the cells of the connective-tissues, and in view of this, and of the fact that Sarcoma is a growth of connective-tissue cells, its appearance presupposes a lesion of a greater degree, and hence more similar to a traumatism, than Carcinoma, which arises in the relatively superficial epithelial-cells. Greater emphasis is therefore given to the local character of cancer by the fact that Sarcoma is practically seldom found in the situations specified in the above table. There is nothing inherent in the nature of the tissues of these parts to preclude the possibility of Sarcoma occurring, and, in fact, Sarcoma does occasionally occur in them, but, with the exception of the skin, they are protected from injuries sufficiently severe to expose the

cells of the connective-tissues, whereas, as already indicated, the living epithelial cells are frequently exposed. Hence, in these situations the carcinomatous type of the disease prevails almost exclusively.

The lesion preceding Carcinoma is largely the result of disease or degeneration, while that of Sarcoma is probably in great measure due to accident: accordingly, Sarcoma in contrast to Carcinoma has no predilection for any site, but appears indifferently in any part of the body. The proportion of cases in the above table which are classified as "not specified", doubtless include a considerable number of the Sarcomatous type, but assuming that all these cases were of this type, it is extremely significant to find that they only comprise about 15 per cent. of the whole. On this basis, Carcinoma appears about three times more frequently in the stomach, or probably even in the relatively minute area of the pylorus, than Sarcoma in all the remaining parts of the body. This fact alone is virtually sufficient to prove that local conditions are of primary importance in the causation of cancer; and it is only one among many others leading to the same conclusion.

Accepting, then, the view that cancer is a local disease, the facts demand that its cause should not only exist in a medium which is common to all the parts primarily attacked, but also that the application of such a medium to any part should bear a proportionate relation to the frequency with which it is attacked. Now, the stomach, uterus, breast, bowel, mouth, and skin are all attacked with great frequency, but in varying de-

grees, and it is evident that, if it is found that all these parts bear a relation to a common medium reasonably proportionate to the frequency with which they are attacked, and if in addition such findings are in agreement with the other facts of cancer, a very delicate and exact test, by which the causative influence of such a medium may be estimated, will be available.

There are certain media, as air, water, and the organic matter of food, which are common to the skin, mouth, stomach, and bowels, but the organic matter of food has no relation to the uterus or the breast and may therefore be excluded from consideration. Air may also be excluded for the reasons, firstly, that it is not compatible with the facts concerning the incidence of cancer on aquatic and terrestrial animals; and, secondly, that it does not coincide with the established facts. If, for instance, air contained the causative agent of cancer, the skin, on account of its greater exposure, should be most frequently attacked; whereas the facts prove that the contrary is true.

Water is a universal medium, and is common to all the organs and parts of the body attacked by cancer, and to all vertebrate animals which are known to be affected by the disease. In view, therefore, that no other universal medium fulfils the required conditions, the conclusion is inevitable that WATER IS THE ONLY MEDIUM IN WHICH THE CAUSATIVE AGENT OF CANCER CAN EXIST.

Before considering the relation of water to various organs, it seems desirable to anticipate certain matters which will be discussed later in greater detail. Firstly,

although cancer is the result of fertilization of a tissue-cell, the manner in which it arises is by no means simple. In reality there are four factors concerned in the process, all of which are essential. They are as follows: (1) a fertilizing element; (2) a living tissue-cell; (3) a lesion exposing living tissue-cells; (4) water. Secondly, the fertilizing elements which are the active cause of cancer are formed by certain protozoal organisms in water, but their numbers, in different classes of water, vary very widely. Thirdly, assuming that all the essential factors are present, the chances of fertilization of a tissue-cell occurring will depend upon: (1) the size of lesion; (2) the number of fertilizing elements present in the water; (3) the length of time in which the water remains in contact with the lesion.

It will, therefore, be realized that the causation of cancer is governed by many conditions, and is in some degree a matter of chance. It is conceivable, for instance, that cancer might originate in the presence of the smallest number of fertilizing elements, the most minute lesion, and the shortest contact with water, and that, conversely, it might fail to arise under the most favorable combination of such conditions; it cannot, however, be doubted that in dealing with a large number of cases the element of chance is neutralized, and may therefore be disregarded.

We are now in a position to consider the manner and degree in which the factors concerned in the causation of cancer are applicable to the established facts of the disease. On the basis of the proposed theory, it is ob-

vious that *primary cancer should appear most frequently in those organs and parts of the body whose contact with water is most intimate and prolonged, and conversely, that it should be rarely found where the presence of water is not a normal event.* Now, by the figures in the above table it is seen that the stomach is liable to attack in a degree far exceeding any other organ. Careful estimates seem to show that cancer appears three times more frequently in the stomach than in any other organ, and that cancer of the stomach constitutes one-third of all cases of the disease. In view of this it is of the greatest significance to observe that the *contact of water with the stomach is more frequent and prolonged than with any other organ.*

Authorities agree that the usual *sites of gastric cancer and gastric ulcer are identical,* and careful observation has recently shown that both gastric cancer and gastric ulcer are not only more common in males than in females, but also *that sex-proportion of the two affections is identical.* Dr. Frank Smithies, in a recent article* on gastric cancer, finds, from an analysis of 712 consecutive cases, that "The sex ratio was approximately that of gastric ulcer: namely, 483 males and 229 females, or 2.1 to 1."

It is interesting to compare the stomach with the duodenum, with respect to their relations to cancer, ulceration, and water. Ulceration of the duodenum is more

*"Symptoms and Signs of Gastric Cancer: an Analysis of 712 Consecutive Operatively and Pathologically Proved Cases." Frank Smithies, M. D., Journal A. M. A., Feb. 20th, 1915.

common than ulceration of the stomach: cancer of the duodenum is seldom seen, while cancer of the stomach is extremely common. At first sight, therefore, it might seem that there is no connection between ulceration and cancer, but it must be remembered that four factors are essential in the causation of cancer. Ulceration supplies two of these factors, namely, a *lesion* which exposes a *living tissue-cell*—the remaining two are: *a fertilizing element,* and its medium, *water.* When the conditions, under which these factors operate in the stomach, are compared with those in the duodenum, a very definite reason will be found for the apparently contradictory relations between ulceration and cancer in each organ, respectively.

Larger quantities of water are retained in the stomach for a greater length of time, and comparatively, in a more quiescent state than in any other organ or part of the body. Thus, conditions in the stomach combine in a manner which is highly favorable to the probabilities of the union of a fertilizing element with a tissue-cell. In contrast to this, water passes through the duodenum, but is not retained, consequently its contact with any lesions which may be present is comparatively brief, and hence the tissue-cells in such a lesion are not exposed to the same number of fertilizing elements, nor for so long a time. Also, owing to the fact that, relatively to the stomach, water in the duodenum flows rapidly through a narrow passage, and so tends to carry the fertilizing elements from the tissue-cells, the chances of fertilization are further minimized. It will now be

seen that, corresponding with the difference in the relation between ulceration and cancer in the stomach and duodenum respectively, there is also a difference in the relation of each of these organs to water; and from the character and proportions of these relations alone there is a strong presumption (virtually amounting to proof, in conjunction with all other considerations tending in the same direction) that *water is the connecting link between ulceration and cancer.*

Reference to the table giving the rates of cancer-incidence on organs and parts will reveal the fact that such important organs as the brain, heart, lungs and kidneys, are conspicuous by their freedom from attack. Doubtless they are included amongst the "not specified" cases, but even estimating their respective rates at the highest point, it is clear that they are remarkably free from the attack of cancer—and from the negative side of the subject this is a point of the greatest value, because it is obvious, that if a theory which purports to explain the high rates of cancer-incidence, is consistent to an equal degree in the opposite direction, its force is doubled.

Now it is a matter of the highest significance that, whereas *all those organs which show the highest rates of cancer-incidence as the stomach, uterus, breast, etc., are freely exposed to water,* all *those in which cancer rarely appears, are, by their anatomical position, absolutely protected from contact with water, under normal conditions.* Hence, with regard to the brain, lungs, heart, kidneys, and other organs and parts, the reasons for their relative freedom from attack, are based on

the same considerations which apply, both generally and particularly, to every manifestation of cancer. In support of this view, nothing is more striking than the manner in which the incidence of cancer on the stomach and lungs, respectively, coincides with the relations of these organs to water. Primary cancer of the lungs is, in contrast to the stomach, extremely rare. The fact, however, that cancer does, at times, attack the lungs is sufficient to show that there is no inherent quality in them which renders them immune to the disease; and evidence that no such immunity exists is supplied by the fact that under some conditions, as, for instance, in the case of the workers in the cobalt mines at Schneeberg, cancer attacks the lungs with unusually great frequency.

The lungs are exposed to a greater number of external influences, and more continuously, than any other internal organ, and the degree to which they are affected, notably in persons of cancerous age, by those conditions which result in lesions of their internal surfaces, and chronic irritations, exceeds that of any other part of the body. No explanation of the comparative freedom of the lungs from cancer is therefore possible on the ground of the absence of the preceding lesions which are an essential factor in the causation of the disease.

Now, if cancer were due to a cause which could affect the lungs and stomach in an equal degree, it should be expected that the frequency with which the lungs were attacked would be much greater than that of the stomach, because the total area of the internal surfaces of the lungs is many times more than that of the stomach.

Since the opposite is true, and since the lungs enjoy no degree of immunity, the conclusion is unavoidable that the greater liability to the disease, which the lungs theoretically should possess, is reversed by the unequal influence of one or more predisposing conditions upon the lungs and stomach respectively, and when the difference in the relations of these organs to water is realized, there will be no difficulty in finding the reason for the high rate of incidence of cancer on the stomach, and its virtual absence in the lungs.

Causation of cancer in the uterus and breast.—For the reason that contact of water with the uterus and breast is required only for cleansing purposes, its relation to these organs is widely different from that of the stomach, in which water is necessary for the performance of its functions. In view of this and of the fact that liability to cancer of the uterus and breast is second only to that of the stomach, it might at first sight appear that the high rates of cancer-incidence on the uterus and breast were disproportionate to, and in disagreement with, the suggested causative connection between water and cancer. It will be seen later, however, that although the uterus and breast are not exposed to water in an equal degree, or with the same regularity as the stomach and some other parts of the body, yet they possess certain anatomical and structural peculiarities, which, in combination with their special liability to lesions, create conditions, favorable to the causation of cancer, by prolonging the action of water upon them.

The uterus and breast undergo rapid atrophy when the period of reproductivity is past. Atrophy implies a diminution of vitality, and diminished power of resistance, protection, and repair, and for this reason these organs, when their functions have ceased, are especially liable to various affections of a degenerative character, many of which are manifested as lesions of their protective surfaces. Cancer may attack the uterus and breast at any age, but it is noteworthy that it rarely appears in them before the period of degenerative change. The cervis uteri, doubtless owing to the special manner in which it is exposed to disease and other injurious influences, is required to exert greater powers of resistance and repair than other parts of the organ; and, consequently, with failing vitality, the manifestations of degenerative changes are more frequent and more pronounced. Hence, the cervix is the seat, primarily, of lesions, and secondarily of cancer, with a degree of frequency far exceeding, and disproportionate to, its size, as compared with the remainder of the uterus.

Under natural conditions there is no reason for contact of water with the uterus, or any other internal part of the generative tract; and, doubtless, there are some persons in whom access of water to these parts has never been required or permitted. Under the present conditions of civilization, however, there is sufficient ground on which to believe that water is deliberately applied to the uterus and contiguous parts with considerable regularity. But water may also reach the uterus, unintentionally, during the ordinary course of bathing, owing

to defects of the muscular mechanism, resulting usually from childbirth. It is a common experience of medical men to find, especially in women who have reached middle-age, disabilities arising from tears, or other injuries of the muscular structures concerned in the process of childbirth. Often such defects have existed for many years without serious inconvenience, but after the climacteric period their effects become more pronounced, mainly because of the failure of muscular power, which accompanies age, and also on account of a general laxity and shrinkage of the tissues resulting from atrophic degeneration. Under such circumstances the natural resistance is absent, or so greatly impaired, that there are no difficulties to the passage of water.

It is to be expected, for the reasons given, that cancer of the uterus should appear more frequently in the married than in the unmarried, and it is therefore satisfactory to find this conclusion is confirmed by the statistical facts. Discussing cancer of the uterus, in the work already mentioned, Dr. Hoffman says: "....from cancer of the uterus the married suffered from a mortality 73 per cent. greater than the single." "The term married, for the present purpose, includes the widowed and divorced."

It is obvious that no large quantity of water can remain in contact with the uterus, but although the quantity is necessarily small, it is important to realize that it cannot be removed by any ordinary means, and also that there is no opportunity for its removal by evaporation. Hence, in the presence of a lesion, *the time al-*

lowed for fertilization to occur is longer than in any other part. Also, a quantity of water small enough to be retained in contact with the uterus remains quiescent and thus increases the effect of prolonged contact in favoring the chances of fertilization occurring.

The cervix is virtually the only part of the uterus exposed to water; it is, also, the seat of degenerative lesion: and it is the part selected by cancer for attack. Now, when it is realized that these three facts bear a constant and proportionate relation to each other, and are also in agreement with the corresponding facts of cancer in all other organs, under the greatest variety of conditions, it will be found impossible to conceive of such a degree of uniform coincidence except on the basis of a coordinating principle common to all.

Cancer of the breast is manifested in the nipple, the lactiferous ducts, and the breast-substance; and as it seems that the causation of the disease in the first, differs somewhat from the two latter, it is convenient to consider them separately.

The skin of the nipple and its surrounding areola, like that of the scrotum and eyelids (all of which are favorite sites of cancer), differs from the skin of other parts by reason of its peculiar thinness and delicacy of texture, and also by the manner in which it is liable to be thrown into deep wrinkles or folds on stimulation. Notwithstanding that it is protected by the clothing, it is extremely liable to fissures and other lesions, any of which may be the starting-point of cancer. It is also subject to various forms of chronic irritation, the best

example of which, in association with cancer, is the eczematous affection known as "Paget's Disease".

That these peculiarities have an effect in rendering this part specially prone to cancer, cannot be doubted. The delicacy of the skin predisposes to lesions from slight causes, and the contractions, by preventing evaporation or ordinary drying, retain water in its folds for an indefinite time, and thus increases the chances for the action of any fertilizing elements which may be present.

Since lesions of the nipple are too remote from the glandular structures of the breast to afford a consistent explanation of the frequency with which cancer appears in the breast-substance, or to coincide with the facts of "duct-cancer", it becomes necessary to consider the conditions concerned in these manifestations of the disease. The lactiferous ducts are the only large ducts which open on the external surface of the body. They converge from all parts of the breast, and having become dilated or ampullated within a short distance of their orifices, meet together within a very small area at the summit of the nipple. The surface of the nipple, at the point where they open, is irregular or verrucose, and is therefore capable of retaining water in its crevices for a considerable time.

Now, even during the period of greatest functional activity, there is little or no resistance to the passage of fluid from the orifices of the lactiferous ducts, and it may, therefore, be assumed that they open and close passively according, on the one hand, to the pressure of

fluid behind them, and on the other, to the general tone of the muscular and other tissues surrounding them. When, however, the functional period has passed, and the tissues are becoming atrophied and flaccid, it is probable that the orifices of the ducts tend to become wider, and their small original resistance more feeble. In such circumstances water might readily enter them by suction, or capillary action; or be forced into them by the pressure of natural movements, during, or shortly after, bathing.

Assuming that a fertilizing element gains an entrance, in the manner suggested, or in some other way, the living cells which line the tract from the orifice of the duct are exposed to its action. The dangers arising from such exposure are very prolonged, and very great, for the reason that a fertilizing element many retain its vitality for a considerable time and may travel by its own motility, or be carried passively to any part. Hence, cancer may occur, either in the duct, or in the substance of the gland, from the same combination of conditions.

On the foregoing basis, it is clear that a proportion should exist between the degree of frequency with which water is applied to the breast and the rates of cancer-incidence upon it. The rates of cancer-incidence are available, and although there are no figures to show the frequency with which water is used, it is, nevertheless, possible to estimate the extent of its use with reasonable accuracy, from a general knowledge of the customs and habits of various races throughout the world. *Cancer increases with the progress of civilization,—and civili-*

zation implies a greater degree of personal cleanliness. The relation between civilization and cancer is not, however, determined solely by personal cleanliness; other factors, the effects of which will be considered later, are concerned in it, but for the present it is sufficient to confine attention to the fact that cancer prevails to the greatest degree in the most highly civilized countries, and especially among persons whose education and social position require the observance of habits of personal cleanliness, and is comparatively infrequent in primitive races and uneducated people. It is therefore to be expected that the rates of cancer-incidence on the breast and skin, should be higher in persons who bathe freely, than in those of careless habits, and it is significant to find that this conjecture is in entire agreement with the actual facts, as established by statistical inquiry.

Double force is given to the foregoing views by the manner in which the national habits of the Japanese people determine the incidence of cancer on the breast and skin. It is well known that extreme personal cleanliness is characteristic of the Japanese. In Japan every person, from the highest to the lowest, takes a bath daily, and it might therefore seem that such free and regular contact with water would result in a very high rate of cancer-incidence on the skin and breast. But the contrary is true: the rates of cancer-incidence on the skin and breast in Japan, are the lowest recorded. The figures (from Dr. Hoffman's work), as compared with those in America are as follows:

	JAPAN		UNITED STATES Registration Area	
	per 100,000 population		per 100,000 population	
	Males	Females	Males	Females
Skin	0.9	0.6	3.5	2.1
Female breast	....	1.8	....	14.3
Stomach and Liver	48.4	31.4	28.8	30.5

The figures for the stomach and liver are only included to show that the Japanese have no racial or other immunity from cancer.

It will be seen that, even in the face of the cleanly habits of the Japanese, the rate of cancer-incidence on the skin and breast are, respectively, nearly four times and eight times less in Japan than in America, and since the Japanese possess no racial advantage, it is obvious that the difference can only be explained by some variation in the conditions under which the disease originates.

The Japanese method of bathing is interestingly described by Professor J. J. Rein in his work on "Japan: Travels and Researches,"* as follows:

"The *cleanliness* of the Japanese is one of his most commendable qualities. It is apparent in his body, in his house, in his workshop, and no less in the great carefulness and exemplary exactness with which he looks after his fields.

"Every Japanese, great or small, takes if possible his warm bath (Yu) every day. The favorite temperature of the water for this purpose varies between 38° and

*"Japan", J. J. Rein, Hodder & Stoughton, 27 Paternoster Row, London.

45° C. (=F. 100-113), and is, therefore, for our sensations, unbearably high.† No one even in an ordinary way bathes in cold or lukewarm water, not even the peasant, though he is accustomed while at his labor to stand for hours barefooted in cold water; nor the Ninsoku (coolie), though he endures the cold of winter half-naked. Only exceptionally, *e. g.*, as a self-imposed penance, or in fulfilment of a vow, is a cold bath taken.

"There is a distinction between private and public baths, both in respect of their internal arrangements and also of the purpose which they serve. In the former the bath (furo) is a pretty deep wooden tub of a blunt, oval form, but much shorter than the body. At its sharper end projects a small sheet-iron flue, which is connected below with a small fire apparatus, and is employed to heat the surrounding water. The furo is placed according to circumstances near the kitchen, or in a separate bath-room (yu-dono) on the side of the court and garden. Towards five or six o'clock in the afternoon, or even some hours later, according to the quantity used, the water is heated, and then used in succession from the master of the house to the humblest servant. In inns the most distinguished visitor has the preference. After the visitors, follow the heads of the family and children; and last come the servants, so that sometimes thirty persons or more one after another use the same water, and the process is prolonged far into the

†High temperatures for warm baths are also common among other Oriental peoples. Thus **e. g.** Kauitz says of the Turks that they are in the habit of bathing in water of 31° R. (39° C.=102° F.) and upwards.

night. The repulsive element of such an arrangement is somewhat lessened when we remember that the process is repeated every day, that soap and other materials that soil the water are not used, the whole consisting rather in a rapid washing down of the body, while an arrangement at the side of the bath gives every one who leaves it the opportunity of washing his face and hands with clean spring water that is not used by anybody else. . . . .

"There are many public bath-houses for the people in every town. The passer-by easily recognizes them by the steam and noise issuing therefrom, for these establishments serve not only the purposes of cleanliness, but those also of entertainment and recreation. Here acquaintances meet each other daily, to smoke their pipes or chat together, before or after their ablutions."

The Japanese method of bathing differs from that of other countries in one particular, important with respect to the causation of cancer, namely, the high temperature at which the water is used. This difference is adequate to account for the relatively low rate, among the Japanese, of cancer-incidence on the skin and breast. Those who are familiar with the conditions under which living organisms exist in water cannot fail to recognize the destructive or retarding effects of high temperatures upon them. It must be understood that the process of cancer-causation has no resemblance to that of other diseases, and that the causative organisms of cancer differ entirely in nature from pathogenic bacteria, and it will appear later that they are so sensitive to changes

of temperature, that variations above a certain degree even in their natural environment are sufficient to prevent their development. Therefore, though it may be desirable, it is not essential that water should be heated to the point of sterilization in order to render it free from danger from these organisms. If allowance is made for some degree of carelessness in the use of water, and for diagnostic and statistical error, it would appear that the temperature of the bath, as used in Japan, is sufficient to reduce the rates of cancer-incidence on the skin and breast to the minimum.

The significance of the low rates of cancer-incidence on *both the skin and the breast* should not be overlooked. These are the only parts of the body in which the rates of cancer-incidence could be largely affected by special conditions and methods of bathing, and the fact that in Japan the rates of *both* vary from the standard of other countries, in a manner consistent with the suggested theory of cancer-causation, is corroborative evidence in its favor of the greatest value.

Precancerous lesions.—As already stated, a preexisting lesion is an essential factor in the causation of cancer. Such a lesion may be defined as: a defect of the internal or external body-surfaces, sufficient to allow access of a fertilizing element to the living tissue-cells. A certain proportion of precancerous lesions are the result of injury, disease, or such congenital defects as nævi, moles, etc.; but these are insignificant as compared with the great majority, which are in reality manifestations of senile, or degenerative, changes.

The living cells of the tissues are most efficiently protected from the invasion of any foreign substance by the intact normal healthy skin and mucous membranes. If, however, from any cause such as injury, disease, abnormality, or degeneration, the integrity of the skin or mucous membranes is impaired; breaches of the surface, which expose the living cells beneath to external influences, are liable to occur, and through them pathogenic organisms (including the causative agent of cancer) gain admission.

It is well known that as age advances all the tissues of the body, but especially the skin and mucous membranes, tend to suffer a loss of vitality which renders them less able to withstand and recover from the effects of the many injurious influences to which they are constantly exposed, and that in consequence, lesions of various kinds are produced, particularly in those parts of the body which are subjected to greater strain or irritation. Further, it has been commonly observed that in some individuals, owing to hereditary predisposition, the degenerations of the tissues associated with age make their appearance earlier in life, and frequently in a more pronounced form than is generally found to be the case. The influence of age and hereditary, therefore, play an important part in predisposing to the disease, or more correctly, to one essential factor in its causation, namely, the precancerous lesion. In this connection it is interesting to notice that the popular belief that "cancer is hereditary", is, in a remote sense, founded upon a basis of truth.

Great emphasis has been laid upon these precancerous lesions by all modern authorities. In a recent article, *"Cancer: its Prevention and Cure", Dr. William J. Mayo, says:

"All vertebrate animals suffer from cancer in situations which are affected by their habits or conditions of life leading to local lesions in the protective mechanism. We must, therefore, look on local lesions as an invitation to cancer, without regard to just what the ultimate cause of cancer maye be. . . . . Bloodgood, in recent years, in a series of remarkable papers on the cancer problem points out that of 820 pathologically fully developed cancers of the skin and visible mucous membranes, he was unable to find a single case with a well-taken history showing the absence of a previous defect which might be looked on as a precancerous lesion. Coley calls attention to the influence of trauma not only in the development of sarcoma, which has been an accepted fact for a generation, but also to the fact that trauma has a strong influence in the production of carcinoma. . . . . Whether the result of mechanical, chemical, or infectious agencies, chronic irritation is the most important of all those precancerous conditions with which we are acquainted, and it is undoubtedly the most potent influence in the development of the disease following congenital lesions and trauma. . . . . It is difficult to obtain evidence as to the appearance of cancer of

*"Cancer: Its Prevention and Cure," William J. Mayo, M. D., Commemoration Volume, American Medical Association.

the internal mucous surfaces of the body, because in the early stage there are, as a rule, no manifestations which lead to a physical examination. Yet we have seen a very considerable number of such early cases and we have observed no instances of early cancer in the mucous membrane of the inner surface of the body which did not show the presence of a previous local lesion. . . . . Bilbroth observed that cancer almost never arises in the normal breast and that it is usually preceded by small lesions of a degenerative character.''

When cases of cancer present themselves for examination, the evidences of preexisting lesions are, not infrequently, obscured or obliterated, and doubtless, for this reason, and because of their apparent insignificance at all times, their importance as a causative factor has, until recently, been largely disregarded. Theory demands the presence of a lesion as a factor of cancer-causation, and the whole weight of general experience and expert observation is added to such demand, with no counter-balancing consideration, hence, it may be accepted as an indisputable proposition that *a preexisting lesion is an absolute condition for the origination of cancer.*

Cancer may arise at the site of *any* lesion, but since the great majority of lesions are never followed by cancer, it is impossible to account for the causation of the disease on the basis of a lesion only. Now, we have already seen that a lesion is only one of four factors essention in cancer-causation, but since it will appear that its practical importance is paramount in the prevention

of the disease, it becomes necessary to consider its relations to the others in detail.

The four essential factors of cancer-causation.—In a strict sense the *cause* of cancer is a fertilizing element, but the knowledge of this, as a solitary fact, is of minor importance in comparison with a correct understanding of the principles which govern the *causation* of the disease. The causative agent of cancer is applied daily in uncountable numbers to some part of the body of every individual, and yet cancer appears in comparatively very few. Now, it is obvious, that if mere contact with the body were the only condition concerned in the causation of the disease, no person or animal could escape, and consequently every species would have long become extinct. Hence, it is clear that the causation of cancer depends, not upon the causative agent alone, but also upon certain factors which are essential to its action, and which together *in combination* may, for practical purposes, be considered as the *true cause* of the disease. Including the causative agent these factors are four in number, and may be reenumerated as follows:

1. A fertilizing element;
2. A living tissue-cell;
3. A lesion of the body-surface;
4. Water.

Water is the medium in which the fertilizing element exists, and by which it is conveyed to the living tissue-cell, and the lesion is the breach or defect of the body-surface, by which the living tissue-cell is exposed to its

action. When the fertilizing element is placed within reach of the living tissue-cell, all the conditions for the formation of cancer are present, and the process has passed beyond the possibility of prevention or control. But since it is only by the application of water to the lesion that the approach of the fertilizing element to the living tissue-cell is rendered possible, it is convenient for the practical consideration of the subject, if the terms "water" and "lesion" be held to signify, in addition to their usual meaning, the presence of the fertilizing element, and the living tissue-cell, respectively.

Conditions which determine the combination of water with a lesion are favorable to the causation of cancer.—Since neither water nor a lesion, acting alone, is capable of causing cancer, though each is a necessary factor in its creation, it is evident, in view of the foregoing, that the disease can only arise from the combined action of both. It is, therefore, to be expected that *the manifestations of cancer should appear in those situations, and with a degree of frequency corresponding to the conditions which determine the combination of water with a lesion.*

Now, it is well known that cancer appears with a high degree of frequency in situations which naturally, or by reason of injury, habit, custom or occupation, are exposed to conditions which favor the production of lesions. For instance, the frequency with which cancer attacks the skin of the hands and face, as compared with the remainder of the skin-surface of the body, is directly proportionate to the degree to which the hands and face

are exposed to atmospheric influences and injuries, especially those arising from occupation, custom or habit. The force of this observation is increased by the fact that there are special forms of the disease, such as "kangri cancer", "chimney-sweep's cancer", etc., which occur in parts of the skin usually protected from exposure, but that in such special cases the part attacked by cancer is always the site of a lesion resulting from *special conditions* of occupation, habit, custom, etc. In kangri cancer, owing to an unusual custom, the skin of the abdomen is injured by heat; and in chimney-sweep's cancer the conditions of a particular occupation predispose to irritation and abrasion of the skin of the scrotum by soot, but from the standpoint of cancer causation there is no essential difference between the lesions resulting from such special customs or occupations, and those which arise from exposure of a general kind. The essential fact is the lesion, and the influences of custom, occupation, habit, etc., are only important in so far as they impair the integrity of the protective surfaces of the body.

But there is another aspect from which the influences of custom, habit, occupation, etc., require to be considered, namely, the manner in which they favor the combination of water with a lesion. At the outset, it must be recognized that habit and custom with respect to the use of water, vary very widely, not only among different races of people, but also among individuals of the same race. Generally it may be said that the use of water is in proportion to the degree of intelligence and

education of individuals, and, doubtless, this is one reason (but there are others) for the lower rate of cancer-incidence on primitive races, and on certain classes of society in civilized communities. In America, for instance, the rate of cancer-incidence on the negro race is always lower than on the white races, and that this is not due to any degree of racial immunity is shown by the fact that the rate of cancer-incidence on negroes in America is higher than on negroes living under more primitive conditions in Africa. It is, therefore, consistent with the facts to assume that the negro race in America has adopted, particularly with respect to the use of water, the customs and habits of civilization to a greater extent than their more primitive relatives, but not to the same degree as the white races. Similar reasons may be applied to the differences in the rates of cancer-incidence on various ranks of society, as, for instance, on the occupied and unoccupied classes, but it is sufficient, without discussion to recognize the fact that *in the presence of a lesion, habit and custom must necessarily, according to their degree, influence the possibility of its combination with water.*

Occupation compels the use of water, both for purposes of cleanliness, and for the reason that the nature of certain trades or businesses demands its employment in processes of manufacture, or in some other way. Its use for personal cleanliness is, for instance, specially required by workers in paraffin, pitch, tar, creosote, soot, etc., not only because of the disagreeable character of such substances, but also because they are liable to cause

irritation or dermatitis of those parts of the skin with which they are in contact. Now, these substances are not readily removed from the skin even when it is normal, but when they are irritated or inflamed the difficulty is greatly increased, and doubtless requires not only a longer exposure to water, but also renders the process of drying the skin painful, and therefore apt to be incomplete. Hence, *contact of water with the irritated parts of the skin is apt to be unusually prolonged.* Such exposure is a daily event, and results, after a longer or shorter time, in cancer at the site of the lesions thus subjected to undue contact with water.

It is interesting to observe that although the circumstances under which paraffin-cancer and similar forms of the disease arise, differ from those of X-ray-cancer, yet the facts concerning the relation of water to the lesions in each case agree perfectly. Workers in X-rays, by daily exposure to their influence, suffer first from dermatitis of the hands, and later from cancer of the same parts. Exposure of the hands to water is, for professional reasons, frequent, and, as in paraffin-workers the same difficulties in drying are created, and consequently the same prolonged contact. Thus, *although the nature of the occupation is entirely different, the same conditions with respect to water and lesions are developed, and are followed by the same form of cancer.*

It is well to realize that there are conditions common, not only to all occupations, but also to the general manner of living, and the facts of cancer demand that such conditions be considered in its causation. Cancer is de-

termined by the manner in which these conditions are combined with relation to an individual, a class, or a community, and the influence of occupation on its causation is *not due to special conditions,* but to *the special manner in which conditions common to all occupations are combined.* Every occupation has some influence on cancer-causation, but it is only in a few special cases that its effects become prominent.

In order to illustrate the manner in which conditions combine to cause cancer, it is appropriate to consider in detail the facts of chimney-sweep's cancer. This form of the disease is the most striking example of cancer-incidence on an occupation, and will serve as an excellent type, not only of occupational cancer-causation, but also of cancer-causation in general.

From figures given in Dr. Hoffman's work it is shown that the rates per 100,000 population for England and Wales, covering the years 1890-92 and 1900-02, of deaths from cancer in chimney-sweeps, as compared with other males of the same age-periods, were as follows:

1890-1892 (per 100,000 population).

	35-44 years of age	45-52 years of age	55-64 years of age	65 years and over
All males	36.6	117.6	276.2	461.7
Occupied males	34.9	112.5	261.0	485.8
Occupied males industrial districts	39.3	123.1	273.5	458.2
Occupied males agricultural districts	31.8	90.7	245.7	493.8
Unoccupied males	105.0	233.1	408.3	417.3
Chimney-sweeps	124.2	532.3	790.3	1,422.2
Ratio chimney-sweeps to all males	3.3 to 1	4.5 to 1	2.8 to 1	3.0 to 1

1900-1902 (per 100,000 population).

	35-44 years of age	45-52 years of age	55-64 years of age	65 years and over
All males	39.9	144.7	362.2	638.3
Occupied males	39.2	141.7	331.1	668.4
Occupied males industrial districts	45.5	154.2	341.1	640.4
Occupied males agricultural districts	28.1	141.5	277.8	675.9
Unoccupied males	71.3	220.0	614.6	591.8
Chimney-sweeps	118.1	286.6	660.8	1,657.9
Ratio chimney-sweeps to all males	2.9 to 1	1.9 to 1	1.8 to 1	2.5 to 1

In these tables the influence of occupation is shown by the high ratio of deaths from cancer in chimney-sweeps to that of all males during the earlier age-periods. During the time covered by these ages men are more actively engaged in their occupations than in the later years of life, and are, therefore, exposed in a greater degree to those influences special to their work which predispose to disease. With increasing age, the effects of degenerative changes, which tend to render the tissues more vulnerable to irritant causes, become progressively greater, and are added to, and intensify the action of those influences which are due to occupation; and were the conditions at all ages in other respects equal, it should be expected that the ratio would increase in a degree corresponding to the increase in age. It is, therefore, of particular significance to find that the contrary is true; that the higher ratios are associated with the earlier age-periods; and it emphasizes strongly that there is a definite relation between the occupation of chimney-sweeping and the causation of cancer.

In England chimneys are swept by means of a flat circular brush, which is introduced from below and pushed upwards, section by section, until it emerges at the top. As the soot is dislodged it falls and is caught in a large bag below. The sweep, however, cannot avoid it, and is usually covered from head to foot.

The classical form of chimney-sweep's cancer affects the scrotum; the principal conditions concerned in its causation are as follows:

1. The skin of the scrotum is extremely thin, delicate, very sensitive to irritation, and *easily injured.*

2. By muscular contraction the skin of the scrotum is thrown into deep folds. *Water, soot, and similar substances, if present, are retained within these folds, and when so retained, their removal is impossible by any ordinary means.* The contracted condition may persist for an indefinite length of time.

3. Owing to its situation and pendulous character the scrotum is subjected to *friction against the clothing and adjacent parts of the body with every movement.*

4. Soot is present on the skin and clothing of chimney-sweeps. Its mechanical action (similar to that of sand or emery), with the aid of friction, *abrades the delicate skin and thus causes lesions.* Chemical action also may possibly assist in the process.

5. The nature of their occupation requires that chimney-sweeps should live in cities. They are consequently entirely exposed to the influence of reservoir-water, which, with respect to cancer-causation, is of greater potency than any other class of water. (This subject is discussed later.)

6. The grimy nature of their occupation requires that chimney-sweeps should bathe the whole body more frequently than any other class of persons. *Lesions of the scrotum are thus regularly exposed to water.*

7. Chimney-sweeps as a class are unable to bear the expense, and do not possess the facilities for heating large quantities of water frequently. *The water used for bathing is therefore seldom heated to a degree sufficient to destroy organic life.*

8. The discomfort and the time consumed in frequent, cold or nearly cold, baths, are good reasons why the process should be hurried through as rapidly as possible. Hence, some degree of *carelessness in drying the skin, especially of the scrotum,* is probable.

9. Owing to the necessity of frequently repeated baths, and to the difficulty of drying the skin of the scrotum, especially when abraded or tender, its *contact with water is prolonged.*

If the foregoing is a fair representation, it would seem to be impossible to find conditions which combine more perfectly to insure cooperation of water with a lesion in the causation of cancer. There is no exposed

part of the body, which by its nature is so vulnerable as the scrotum, or which allows of equal opportunities for the action of water upon it. When it is realized how far the scrotum is removed from the influences of ordinary occupations, it must seem incomprehensible that the occupation of chimney-sweeps should supply the conditions, which of all others are best adapted for the production of lesions, and for their association with water in a part of the body which ordinarily is little liable to the attack of cancer, but which in chimney-sweeps is attacked with extraordinary frequency, unless a relation between the association of water with the lesions, and the causation of cancer, is recognized.

The significance of the conclusions concerning "chimney-sweep's cancer" are greatly increased by the fact that it has been shown that the basis upon which they are founded is common to all other manifestations of the disease which have been considered herein. The examples given are comparatively few, but they cover too wide an area to leave room for reasonable doubt that the principles enunciated in connection with them will be found to be equally consistent with the manner under which all other manifestations of cancer arise.

PART III

There is another side to the subject of cancer-causation, presenting features of an entirely different character from those already examined, which it now becomes necessary to consider. Hitherto, for the reason that their consideration opens up a field of inquiry which it is convenient to consider independently, little has been said concerning two of the essential factors of cancer-causation, namely, water and the fertilizing element.

Water and the fertilizing elements are so intimately associated that their influence in cancer-causation may, for practical purposes, be considered as governed by conditions which concern water alone; but in order to understand certain variations on the cancer-causing potency of water, some knowledge of the organisms from which the fertilizing elements are derived is required.

It will be remembered that in discussing the question of fertilization it was suggested that a tissue-cell may be regarded theoretically as an independent unicellular organism; and that reasons were given in support of the view that fertilization is possible between a tissue-cell and the male element of an organism of a corresponding developmental rank, but that it was not possible in the case of species higher in the scale of evolution. Hence, in accordance with this view, it is unnecessary, in searching for the fertilizing element, to extend the range of inquiry beyond the limits of unicellular organisms or Protozoa.

The Protozoa.—The characteristics of the simplest forms of life are so rudimentary that distinction between plant and animal species cannot always be made, and owing to this absence of differentiation, it has been found impossible to classify these organisms clearly; hence the terms which are applied to them are often confusing. The term "Protozoa" has been applied to a class of unicellular organisms, but since it is also commonly used in a larger sense to include *all organisms of the simplest type,* it is convenient for the present purpose to attach this latter meaning to it.

A large number of facts concerning these organisms are outside the range of the present purpose. Only those matters which have a bearing on cancer-causation require to be considered. The whole subject is excellently dealt with by Professor George C. Whipple, in his work,* "The Microscopy of Drinking Water," which is the authority for the statements here given, and to which reference may be made for fuller information.

Protozoal organisms are simple masses of protoplasm, generally of microscopic size, existing singly, or if in groups, without individual differentiation. Many thousands of species are known to exist, and are mainly distinguished by their form, color, markings, presence of chlorophyll, method of locomotion, and the possession of cilia, flagellae, and other rudimentary structures. Some species belong to the plant kingdom and others to

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*"The Microscopy of Drinking Water", George C. Whipple. John Wiley & Sons, New York.

the animal kingdom, but between these there is a third group, the nature of which it is impossible to determine.

Our knowledge of the reproduction of protozoal organisms is very imperfect; various forms of sexual and asexual methods are described, but for the present purpose it is sufficient to consider certain cases of sexual reproduction only. In those species where it is possible to distinguish between the sexes, the female organism differs in no apparent respect from any individual typical of the species; the male organism is entirely different, and except in size may correspond generally in form and parts to the spermatozoa of the higher animals. In the case of the Chloroplyceæ, Prof. Whipple describes the reproductive processes as follows: "Reproduction takes place either asexually, *i. e.*, without the aid of fecundation, or sexually. There is but one general method of asexual reproduction, namely, the formation within the cell of spores, which become scattered and give rise to new cells. There are three general types of sexual reproduction. The simplest is the formation in the cells of zoospores, which become liberated and ultimately copulate with other zoospores. Two of these zoospores become attached by their ciliated ends, their contents become fused, and a zygospore results. After a period of rest zygospore may develop into a new plant, or may break up into other spores. The second type of sexual reproduction is known as conjugation. Two cells come in contact, and by means of openings in the cell-walls their contents become fused. A zygospore (sometimes two) is formed, which after a period of rest, gives rise

to new plants. The highest form of sexual reproduction takes place by the formation of a rather large female oospore, which becomes fertilized by small male cells.''

The foregoing supplies evidence, sufficient for the present purpose, of the presence of fertilizing elements in water. The function of spermatazoids is well-recognized, but in view of a natural tendency to associate them with fertilization exclusively, it is proper that the possibility of fertilization by other agents should not be overlooked. There is no reason to believe that fertilization may not occur with equal readiness by conjugation or by zoospores, or even by the action of agents which, in the imperfect state of our knowledge, are at present unsuspected. The form of the fertilizing element is not, however, a matter of primary importance in the theory of cancer-causation. It is sufficient, irrespectively of any other consideration, that the existence in water of a fertilizing element which was postulated on theoretical grounds, is verified by actual observation.

Water and Protozoa.—Protozoal organisms are found in water everywhere throughout the world, and though their distribution is not equal in every part they are rarely absent from any class of water as commonly used. As water is the medium in which they exist, their growth and development is affected by the conditions to which water is exposed. Some of these conditions are local in their effects, as, for instance, the presence in water of chemical substances, introduced accidentally or for purposes of purification, but with respect to their influence on cancer-causation such conditions are not of major im-

portance. Cancer is a universal phenomenon, and can only be largely affected by widely-spread influences, and from this viewpoint of its causation it is important to observe that the conditions with universal effects upon the growth and development of protozoal organisms are: light, nitrogenous food-material, temperature and quiescence.

It now becomes necessary to consider the manner in which the effect of these conditions is reflected through protozoal organisms upon cancer-incidence. For this purpose it is convenient to divide water, according to its relation to these conditions and to protozoal organisms, into four classes, as follows: (1) Tropical waters. (2) Flowing waters. (3) Still or stagnant waters. (4) Ground waters.

1. Tropical waters differ from those of other climates, in a large degree, only by reason of their higher temperature. Contrary to previous expectations, the effect of this is a *diminution in the number of protozoal organisms in the warm waters of the tropics as compared with the waters of colder regions.* The facts concerning the influence of temperature upon the duration of life and the density of pelagic organisms are stated and discussed in the work of Dr. Jacques Loeb, to which reference has already been made, as follows: "It has often been noticed by explorers who have had a chance to compare the faunas in different climates that in the polar seas such species as thrive at all in those regions occur, as a rule, in much greater density than they do in the moderate or warmer regions of the ocean. This

refers to those members of the fauna which live at or near the surface since they alone lend themselves to a statistical comparison. In his account of the Valdiria Expedition, Chun calls special attention to this quantitative difference in the surface fauna and flora of different regions. 'In the icy waters of the Antarctic, the temperature of which is below 0° C. we find an astonishingly rich animal and plant life. The same condition with which we are familiar in the Arctic seas is repeated here, namely, that the quantity of plankton material exceeds that of the temperate and warmer seas.'

"And, again, in regard to the pelagic fauna in the region of the Kerguelen Islands, he states: 'The ocean is alive with transparent jelly-fish, Ctenophores (Bolina and Callianira), and of Siphonophoræ, colonies of the genus Agalma.'

"The paradoxical character of this general observation lies in the fact that a low temperature retards development, and hence should be expected to have the opposite effect to that mentioned by Chun.

"The writer believes that this paradox finds its explanation in experiments which he has recently made on the influence of temperature on the duration of life of cold-blooded marine animals. The experiments were made on the fertilized and unfertilized eggs of the sea-urchin, and yielded the result that for the lowering of temperature by 1° C. the duration of life was about doubled. Lowering the temperature by 10° therefore prolongs the life of the organisms over a thousand times, and lowering by 20° prolongs it about one million times.

Since this prolongation of life is far in excess of the retardation of development through a lowering of temperature, it is obvious that, in spite of the retardation of development in the Arctic seas, animal life must be denser there than in the temperate or tropical seas. The excessive increase in the duration of life at the poles will necessitate the simultaneous existence of more successive generations of the same species in these regions than in the temperate or tropical regions.''

The foregoing observations, both with respect to the general and experimental results, are of the greatest value. Retardation of development by cold is doubtless an important reason for the greater density of organisms in cold waters, but if it is assumed that organisms develop to the maximum degree permitted by the conditions of their environment (and there is no reason to suppose that such an assumption is less applicable to the case of warm regions than to that of cold) it will not appear that accelerated development is the full explanation of the facts concerning the lighter density of organisms in warm waters, and it therefore becomes necessary to consider the influence of temperature upon their environmental conditions.

Doubtless for the reason that they require sunlight the natural position of most species of protozoal organisms is at or near the surface of the water. At a short distance below the surface their numbers decrease rapidly, and, as the depth becomes greater, continue to diminish until they almost disappear. From this it is evident that their existence depends upon *their ability*

to maintain themselves near the surface of the water, and that any interference with their power to do so will tend to result in a diminution of their numbers.

Concerning the ability of organisms to remain at the surface, Prof. Whipple says:

"The viscosity of water has an important influence on microscopic organisms, as it materially affects their flotation. It also affects the sedimentation of fine particles in the water and even the circulation of the water itself. Viscosity varies with the temperature. It is twice as great near the freezing-point as at ordinary summer temperatures. It is shown by the table:

VISCOSITY OF DISTILLED WATER AT DIFFERENT TEMPERATURES.

Temperature C.	Viscosity Co-efficient (Dynes per sq. Centimeter.)	Percentage of Viscosity at 0° C.
0°	0.017780	100.0
5	0.015095	84.9
10	0.013025	73.2
15	0.011425	64.2
20	0.010015	56.3
25	0.008910	50.1
30	0.007975	44.8
35	0.007200	40.5
40	0.006535	36.8
50	0.005475	30.8
60	0.004680	26.3
70	0.004060	22.8
80	0.003560	20.0
90	0.003155	17.7
100	0.002830	15.9"

It is, therefore, hardly possible to doubt that lowered viscosity of water is an important additional reason for the diminished density of protozoal organisms in tropical regions. The effects of the conditions thus created are regular and uniform according to temperature, and are tirely compatible with the maximum development of organisms in the environment thus created.

Before these conclusions can be applied to the question of cancer-causation reliable data are necessary to show the influence of temperature upon cancer-incidence. Such data are given by Dr. Hoffman in the figures reproduced below:

MORTALITY FROM CANCER IN CITIES ACCORDING TO LATITUDE, 1908-1912.

No. of Cities.	Degrees of Latitude.	Mean Annual Temperature.	Rate per 100,000 Population.
35	60 N.-50 N.	48.0°	105.7
48	50 N.-40 N.	53.3°	92.4
24	40 N.-30 N.	58.5°	78.1
7	30 N.-10 N.	72.5°	42.3
4	10 N.-10 S.	74.6°	40.9
7	10 S.-30 S.	65.9°	37.7
5	30 S.-40 S.	62.7°	89.8
130			Average 91.0

A study of these figures will show that there is a fixed relation between temperature and cancer virtually throughout the world. A fixed relation of this kind implies the action of a *uniform principle*: but it implies much more; namely, that *cancer and its cause are confined within the limits of their relation to temperature.*

This narrows very considerably the field of cancer-inquiry, and thus negatives absolutely many suggested causes as possibilities.

The relation of cancer to temperature is inverse, and it has been shown that the relation between temperature and water and protozoal organisms, especially in regard to the *degree of their cooperation,* is also inverse. In view of this, and of the universal distribution, and the diverse character of the manifestations of cancer, no one can fail to recognize that the perfect manner in which the relations of temperature, water, protozoal organisms, and cancer coincide, is remarkable, and of the highest significance.

Flowing-waters.— Water may be set in motion by gravity, as in rivers and streams; by wind-action over large surfaces, as on the Great Lakes; and mechanically, as in pumping, and various other processes for its distribution and purification. Movement retards the growth of protozoal organisms in water; it may, if sufficiently violent, result in a disintegration of their delicate structure, or it may cause their dispersion.

In order that they should reproduce themselves to the fullest degree, it is necessary that protozoal organisms should congregate together and remain in the neighborhood of an abundant food-supply. Movement in small lakes and ponds is never sufficient to injure them, and, owing to the narrow area in which they are confined, their dispersion is impossible; but in the Great Lakes and in rivers, not only are they subjected to increasing movement, but also, there is no limit to the extent to

which they may be carried from their main food-supply, and scattered apart from each other. Hence, in moving waters the conditions for their development are very unfavorable, and, though the statement is liable to exceptions, it may be said their numbers in waters of this class are few as compared with those of still or stagnant waters. And also, for the same reasons, it is to be expected that the number of organisms in rapidly-flowing rivers should be fewer than in rivers which are sluggish, and tend to stagnate in certain parts of their course.

Now, since the number of protozoal organisms in water is governed by the rapidity of flow, it becomes possible on this basis to test the relation of protozoal organisms to cancer. If a causative relation exists between protozoal organisms and cancer, it is obvious that *cancer should prevail to a greater degree in those parts of a country where water tends to stagnate, than in those parts where, owing to the physical characters of the country, the opportunities for stagnation are reduced to the minimum.*

For the purpose of comparing the foregoing conclusion with the statistical facts of cancer-distribution, the United States of America offers the greatest advantages, for the reason that reliable statistical data are available, and also because the size of the country and the diversity of its physical characters, renders it possible to divide it into certain well-defined regions. According to its salient features the United States may be regarded as a central, wide, flat valley, which rises on

each side to join the ranges of the Appalachians toward the east, and the Rocky mountains in the west, and from the summit of which ranges the line of the country slopes gradually downwards to the ocean on either side. There are two great watersheds, each draining towards the central plain on one side and the ocean on the other. The fall on each side must necessarily be more or less rapid, but the flow of water on reaching the plain cannot fail to become sluggish, or in parts reduced to the point of stagnation.

In addition to the foregoing there are features peculiar to the New England States which require to be noticed. At some former period this part of the country was subjected to glacial action which has resulted in an extraordinary number of lakes. The State of Maine alone contains over 1600, with a total area of more than 2000 square miles. Altogether the States of New England cover an area of 66,424 square miles, of which 4,448 square miles are water. Stagnation of water reaches its highest degree in small lakes, ponds, and reservoirs, and in view of this it can be readily understood that the presence of such an enormous quantity of stagnant water throughout the New England States is a condition highly favorable to the development of protozoal organisms and hence to the causation of cancer.

According to such physical characteristics the United States as a whole may be considered with respect to the incidence of cancer in four divisions, which in the order of their influence on cancer-causation as anticipated theoretically, may be enumerated as follows:

1. The New England States.
2. The Central States.
3. The Rocky Mountains region.
4. The Appalachian region.

The twenty-four States included in the United States Registration Area are arranged below, according to their rates of cancer-mortality. This arrangement is adopted in order to show the regular manner in which the incidence of cancer falls upon, and groups together States which have the same physical characters. Each group is numbered according to the number of the division, as indicated above, to which it corresponds. The figures are taken from the Mortality Statistics, Fourteenth Annual Report of the Census Bureau, for the year 1914. They are as follows:

RATES OF CANCER-MORTALITY IN THE STATES OF THE U. S. REGISTRATION AREA PER 100,000 OF POPULATION.

General Average rate, 78.9.

1	Vermont	111.7
	Maine	107.5
	New Hampshire	104.4
	Massachusetts	101.4
	California	97.6
1	Rhode Island	93.3
	New York	87.8
	Connecticut	85.1
	Maryland	82.8
2	Ohio	81.8
	Michigan	81.5
	Indiana	81.1
	Wisconsin	78.5

	New Jersey	78.4
	Minnesota	75.1
	Pennsylvania	72.2
	Missouri	67.1
3	Washington	53.5
	Utah	52.1
	Colorado	50.7
	Montana	49.4
4	Virginia	48.4
	Kentucky	48.0
	North Carolina	47.9

When thus arranged in the numerical order of their respective cancer mortality-rates it is seen that there are only five States which do not fall into some group. The reason for this in the case of four, namely, New Jersey, Minnesota, Pennsylvania and Missouri, is that these States represent the general average of the whole. It is to be observed that they fall together in a group between the characteristic groups, and their cancer-rates are reasonably consistent with the general average rate.

California is therefore the only State which really stands alone, and there are several reasons why this should be the case. California covers a wider range of latitude than any other State, and is unique among them with respect to the variety of its physical characters and climate. The average annual rainfall varies from 0-10 inches in the southern parts to 60-70 inches in the northern parts of the State. The year is divided sharply into wet and dry seasons, yet, notwithstanding this, the same reliance, as in other States, can never be placed upon the appearance of rain at any time or season.

Owing to this uncertainty it is necessary to anticipate periods of drought by providing for the storage of water in sufficient quantity to insure against a shortage in the public supplies. Water thus stored for long periods, by reason of the growth of protozoal organisms in it, becomes highly potent in the causation of cancer; and since a large proportion of the population of the State is urban (43.3% of the population were congregated in 11 cities in the year 1910), a tendency toward a high cancer-rate must always be present.

The regularity with which the cancer rates of the remaining nineteen States corresponds with the physical characters of each is strong evidence of the influence of the principle, already suggested, concerning the relation of water to the causation of the disease. It is inconceivable, except on the basis of such a principle, that the distribution of cancer as shown by the figures of each of the above groups of States, could coincide so exactly with definite regions of the country according to their physical characteristics.

The value of this feature of cancer-distribution cannot be disregarded even though it stood alone; but it is to be remembered that it is only one of many features of equal or greater value, each of which combines symmetrically with the others in the design of cancer-causation.

Stagnant waters.—The growth of protozoal organisms reaches its maximum in ponds, small lakes, reservoirs, or any body of water which remains in a state of quiescence for long periods of time. Such waters are

freely exposed to sunlight; are little affected by wind action or other disturbing influences; and generally contain a plentiful supply of nitrogenous matter suitable for the food of protozoal organisms.

For these reasons stagnant waters are of the highest potency in the causation of cancer, and since, under existing conditions, a constantly increasing proportion of the population in all civilized countries is being exposed to the "menace of cancer", by reason of the fact that these waters are the source of most public water-supplies, the recognition of the existence of such a danger, and of the means by which it may be avoided, is urgently necessary.

For practical purposes it may be considered that all water, unless artificially treated, contains organic life and nitrogenous and other impurities. The degree, however, to which such impurities are present in reservoir-waters depends partly upon the nature of the original source, and also upon the character of the reservoir itself. Certain sources are relatively pure or impure, and some reservoirs are especially liable to become foul, but for the present purpose it is not necessary to consider these points in detail. It is sufficient to recognize that there are considerable differences in the quality of various reservoir-waters, and in the number of protozoal organisms in them.

The following table from Professor Whipple's work, shows the variations in the numbers of protozoal organisms:

LAKES CLASSIFIED ACCORDING TO THE INDEX OF FREQUENCY.

	Group I.	Group II.	Group III.
Number of Lakes and Reservoirs in the Group	28	18	20
Limits of Frequency Index	0-25	25-50	50-100
Average index of frequency	12	39	78
Organisms per C. C. mean yearly average	362	776	1410
Organisms per C. C. minimum yearly average	54	441	984
Organisms per C. C. maximum yearly average	1413	2800	3090
Organisms per C. C. mean average for 4 summer months	414	1023	1965
Organisms per C. C. minimum average for 4 summer months.	66	227	985
Organisms per C. C. maximum average for 4 summer months.	1058	4588	7659

Water is seldom supplied direct from the reservoirs to the consumer without attempts being made to render it as free as possible from living organisms and other forms of impurity. Various methods of purification are used, according to the character of the water to be treated, and though there are considerable differences in the details of each system, some form of filtration, with or without coagulation, chemical disinfection, and aeration is used in all. After treatment the number of organisms is greatly reduced, but no system has yet been devised which can be relied upon to render water entirely free from them, and if after purification water is stored in

an open reservoir an increase in their number is practically certain to occur. Concerning this point, Mr. Allen Hazen, in his very instructive book* "Clean Water and How to Get It," says:

"There are many cases where such waters are stored in open reservoirs; in these cases the waters always deteriorate in quality, but not always to the extent of making them unacceptable. Deterioration takes place principally in warm weather. It results from the growth of microscopic organisms in the water."

The effect of storage on the growth of organisms is shown by Professor Whipple in the following table:

MICROSCOPIC ORGANISMS PER C. C.

Date 1903.	Raw Water.	Filtered Water After Storage.
April 23	60	1,455
May 11	70	135
June 8	95	65
June 20	65	130
July 8	205	655
July 23	230	2,440
August 6	185	2,265

Professor Whipple proved that organisms actively grow on the sand surface of an open filter. In some cases their numbers amounted to several millions per square centimeter. His researches also show that organisms have a tendency to decrease in water pipes. From weekly observations, extending over five years (1891-5),

*"Clean Water and How to Get It," Allen Hazen, John Wiley & Sons, New York.

he found the average number of organisms per cubic centimeter as follows:

Chestnut Hill Reservoir	248
Brookline Reservoir	215
Tap in Park Square	189
Tap in Mattapan	81

Concerning his observations on the growth of organisms in water-pipes near the Chestnut Hill reservoir he says:

"These brought out the fact that sponges and the Bryozoa were well established in the pipes. Many other organisms were also observed. In some places almost pure cultures of Stentor and Zoothamium were found. At other points hosts of different organisms were seen, such as snails, mussels, Hydra, Nais, and Anguillula, Acineta, Vorticella, Arcella, Amoeba, countless numbers of ciliated infusoria and many other forms. The growths were distinctly animal in their nature, but in many places parasitic vegetable forms, such as Achlya, Crenothrix, Leptothrix, etc., were common. The most important class of organisms found, however, was the Bryozoa, of which Fredericella and Plumatella were the chief representatives."

Since there is no reason to suppose that the average conditions in cities throughout the country differ materially from those represented by the foregoing investigations, it would appear that it is practically impossible to supply water to large communities free from protozoal organisms. Professor Whipple's observations show that, even after purification, water is liable to

contamination in the water-pipes, and to a fresh growth of organisms during the period of storage. On the basis of his figures there is in water as delivered to the consumer an average of 135 organisms per c. c.: approximately equal to 69,000 in each pint. This number does not, however, fully represent the cancer-causing potency of the water, since, owing to the activity of the reproductive processes in these organisms, the number of spermatozoids or other fertilizing elements must necessarily be many times greater.

Urban and Rural cancer mortality-rates.—In all countries urban cancer mortality-rates are higher than rural, and in the light of the dangers of reservoir-water, it is to be expected that this should be the case. The *whole population* of a city is exposed to the influence of reservoir-water, whereas *in rural districts only a limited proportion of the population is exposed to the danger of any single source of water-supply.* In rural districts certain sources of water-supply, as for instance those drawn from ponds, lakes, or the stagnant waters of rivers, may equal or even exceed reservoir-water in cancer-causing potency, but, while available to those in the immediate vicinity, such sources of supply, by reason of distance, are usually unavailable to the greater part of the community. It is interesting to observe that the prevalence of cancer in valleys and in "cancer-houses" is consistent with the foregoing view. Concerning rural water supplies it cannot be doubted that as a whole they are safer than urban supplies, if only for the reason that a large part of the supply is drawn

from ground-waters, which of all classes of water are the least potent in the causation of cancer.

The progressive increase of Cancer.—There is a tendency, in all *civilized* countries, towards an increase in the rates of cancer-mortality. In some countries, *e. g.,* The United States of America, the increase has been rapid, while in others where the cancer mortality-rates are highest, as for instance in Switzerland, it has been supposed that the maximum point has been reached, and that further increase is impossible. Such a view clearly implies an impossibility. Theoretically the maximum point of cancer-incidence implies the maximum degree of exposure to the causative agent, that is, continual exposure of the whole population to water of the highest cancer-causing potency. Such conditions, even in the case of the smallest community are almost inconceivable, and throughout a country are obviously impossible. In any country the *rate of cancer-incidence is always the maximum for the* CONDITIONS WHICH DETERMINE THE DEGREE OF EXPOSURE *of its population to the causative agent of the disease.* Hence, changed conditions must necessarily result in changes in the rate of cancer-incidence.

Although the increase of cancer in the United States has been rapid, the mortality-rate of the disease has not yet reached the point attained in many European countries by a slower rate of increase over a longer period. The reason for this is obvious on the basis of a causative relation between reservoir-water and cancer. In Europe the growth of cities, and hence of reservoirs, has

been determined mainly by the natural increase of the population, and consequently, although in many countries it has reached a high state of development, its progress as compared with that of the United States has never at any time been rapid. On the other hand, the growth of American cities has been due, in a very large measure, to immigration of Europeans, mostly of reproductive ages. The effect of this has been not only a remarkably rapid development of cities in the United States, but also a corresponding retardation of those in Europe. Owing, however, to the size of the country, the density of population, and the ratio of the total urban population to the whole it is not yet so great in the United States as in many European countries. Hence, for the reason that a smaller proportion of the population is exposed to reservoir-water the average cancer mortality-rate in America is lower than that of many European countries, notwithstanding the greater rapidity of its progressive increase.

As cities multiply the differences between rural and urban life tend to diminish. Many rural inhabitants have business interests which compel them to spend a great part of their time in some convenient city, and of the others there are probably few who do not avail themselves of the present-day facilities for travel in order to participate, socially or otherwise, in city life. Thus a greater proportion than formerly of the rural population are exposed to the dangers of reservoir-water, and consequently tend to suffer from cancer in a corresponding degree.

No country in Europe can equal the record of the United States either for urban development, or for the extent and rapidity of increase of its facilities for travel, and in view of the importance of these two factors, as indicated in the foregoing, there is little room to doubt their influence upon mortality-rate of cancer.

Ground-waters.—For the reason that light is necessary for the growth of protozoal organisms they are, theoretically, unable to develop in ground-waters, though in practice, owing doubtless to defective conditions, they are not uncommonly found to exist. Generally, however, their presence is to be considered as abnormal.

When ground-waters are exposed to sunlight they become in effect surface-waters, and owing to the large amounts of nitrogenous and mineral substances which they hold in solution, the growth of protozoal organisms in them exceeds in rapidity and vigor that of any other class of water.

Ground-waters exposed to sunlight by storage in open reservoirs, or in any other way, thus lose their characteristics, and since such exposure is commonly practiced, the value of conclusions, which should otherwise have been considerable, concerning their relation to cancer-causation, are thereby greatly impaired. The lower average of the rural cancer mortality-rate, as compared with the average urban rate, is doubtless due in part to the wide use of ground-waters in rural districts. But in the case of cities in which ground-waters are the source of supply, the data concerning the character of the water as delivered to the consumer are not

sufficient to render a comparison between them of value. The facts concerning the water-supply of the City of Memphis are of such an exceptional character that their relation to the cancer mortality-rate of the city is deserving of some notice. Memphis draws its supplies from its world-famous artesian wells. These wells are more than eighty in number, with an average depth of 400 feet. They yield an abundance of excellent water. The average cancer mortality-rate throughout the United States Registration Area, for the year 1913, was 78-9 per 100,000 population. The corresponding rate for the City of Memphis was 54.9; *the lowest recorded of any city of equal size in the country.*

But there is a difference between ground-waters and surface-waters not only with respect to protozoal organisms, but also to all those forms of organic life which, by reason of certain characteristics peculiar to their order, are grouped together under the term "Fungi". It is estimated that there are more than 30,000 species of fungi, but accurate knowledge of the subject is not yet forthcoming. The Schizomycetes or Bacteria have by some authorities been regarded as species of fungi, and on account of certain characteristics which they possess in common with all other species of the order, this mode of classification may, for the present purpose, be considered valid.

Fungi are sharply differentiated from other forms of organic life by their power to grow in the dark. Not only is sunlight unnecessary for their development, but is in ordinary degrees of intensity fatal to them, and

doubtless, it is for this reason that certain fungi, as for instance Crenothrix, Leptothrix and others, are rarely present in surface-waters, though they are able to grow vigorously in water-pipes, wells, and all waters stored in the dark.

Now, owing to the inability of fungi to develop in the presence, and of protozoal organisms in the absence, of sunlight, it follows that their numbers in water will vary according to its exposure or non-exposure: surface waters will afford the best conditions for protozoal organisms; ground-waters for fungi, and conversely. Hence, in all classes of water *the numbers of protozoal organisms and fungi must vary according to an inverse relation* determined by the action of sunlight upon them.

Inverse relation between protozoal organisms and typhoid bacilli.—Typhoid bacilli belong to the Schizomycetes or Bacteria, and therefore should theoretically bear the same relation to protozoal organisms as Fungi in general. No organism has received more careful investigation, especially in connection with water-supplies; and for this reason the consideration of certain facts concerning it is peculiarly appropriate to the present purpose.

Experiment has shown that in sewage and ordinary water, typhoid bacilli tend to die out quickly: the duration of their existence depends upon the number of other organisms present—*the more organisms, the more quickly they die out.* In *sterilized* water they live for about a month. In *sterilized* soil they have remained alive

for more than 400 days. Exposure to *direct sunlight kills them in a few hours.*

The salient point is that the existence of typhoid bacilli is governed by the two factors—sunlight and protozoal organisms. In view of the difference, with regard to these two factors, between surface-waters and ground-waters, it is to be expected that a corresponding difference should exist in the numbers of typhoid bacilli respectively present in them. The results of direct observation on this point are given very clearly by Professor W. P. Mason in his valuable work,* "Water-Supply," as follows: "One important point to be remembered is the antagonism between the disease germ and the common bacteria† so largely found in surface-water. While such antagonism has been broadly noticed, Percy Frankland has placed the demonstration in the following form. He introduced typhoid bacilli into deep well-water which was almost wholly free from bacteria,† into Thames water which contained a large number, and into Loch Katrine water in which the number was intermediate between the two. He found that the typhoid bacilli died off more rapidly in the Thames than in Loch Katrine water, while they persisted longest in the sparsely populated deep well-water. Thus the longevity of these pathogenic bacteria was inversely proportional to the bacterial† population in the waters into

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*"Water-Supply," Professor W. P. Mason, John Wiley and Sons, New York.

†The context renders it clear that the term "bacteria" is here used as synonymous with "protozoal organisms" or "protozoa".

which they were introduced. Thus we see that a relatively pure stream, if a rapid one, might carry infection over long distances."

To the same effect Professor Whipple says: "Sedimentation is only one method by which the bacteria in the river are removed from the water. Another important factor is their destruction by larger microscopic organisms. These microscopic organisms, algæ, protozoa, rotifera, crustacea, etc., play an important part in the self-purification of the Genesee River during warm weather. A somewhat extended study of these organisms was made. Samples for microscopical examination were collected on different days at various points between the East Side Trunk Sewer and the lake at the surface, mid-depth and bottom. The variations in the relative numbers of the organisms of these different groups at various places in the river below the East Side Trunk Sewer illustrate in a typical way the biological action involved in the self-purification of a stream.

"Immediately below the outlet of the trunk sewer there was a zone of heavy pollution within which the numbers of bacteria were very high, but the crustacea relatively low. Below this point of maximum bacterial life, the numbers of bacteria decreased to the lake. In the vicinity of the intense bacterial pollution and for a short distance below it, the numbers of protozoa were high, as might be expected from the fact that these organisms consume bacteria as food. At the same time there was a slight increase in the algæ, and their numbers were well maintained down-stream to the river mouth."

This evidence is too precise to admit of a doubt that, on the positive side, the relation of protozoal organisms to typhoid bacilli is of the most rigid character. On the negative side it remains to be determined whether the absence of protozoal organisms from water is followed by the multiplication of typhoid bacilli. Conclusive evidence on this point is given by Professor Whipple as follows:

"**Increase of bacteria after copper treatment.**—A secondary effect of the copper treatment is to increase the number of bacteria in the water. This has been observed so often that it may be considered as a universal phenomenon. The following figures by Jackson illustrate this bacterial increase. They refer to one of the reservoirs of the water-supply of Brooklyn that had been treated with copper to destroy a growth of Asterionella.

EFFECT OF COPPER SULPHATE ON WATER BACTERIA AFTER A REDUCTION OF ASTERIONELLA

Date	Number per Cubic Centimeter: Microscopic Organisms	Number per Cubic Centimeter: Bacteria
March 13, 1905—Before treatment	4,625	405
March 14, 1905—After treatment	3,645	600
March 15, 1905— " "	3,325	6,000
March 16, 1905— " "	1,925	11,000
March 17, 1905— " "	1,850	12,000
March 18, 1905— " "	1,575	45,000
March 20, 1905— " "	1,350	100,000
March 21, 1905— " "	900	440,000
March 22, 1905— " "	350	630,000
March 23, 1905— " "	350	310,000
March 24, 1905— " "	400	107,000
March 25, 1905— " "	360	80,000
March 26, 1905— " "	300	64,000
March 27, 1905— " "	270	50,000
March 28, 1905— " "	150	37,000
March 29, 1905— " "	100	20,000
March 30, 1905— " "	100	8,000
March 31, 1905— " "	60	3,500
April 1, 1905— " "	28	860

"Sometimes the numbers of bacteria are even higher than those given in the table."

In view of these results it must be conceded that the evidence in proof of an inverse relation between protozoal organisms and typhoid bacilli is conclusive. Now, in the face of this relation, it is obvious that, in so far as typhoid-fever is a water-borne disease, it should prevail according to the character of each class of water as determined by the predominance of protozoal organisms

or typhoid bacilli. That is to say, the greatest prevalence of the disease should be associated with those classes of water in which the fewness of protozoal organisms allows typhoid bacilli to predominate; and on the other hand typhoid-fever should prevail least in association with waters in which the numbers of protozoal organisms are greatest. It has already been shown that protozoal organisms are few in ground-waters, and numerous in surface-waters according to each class; also that the numbers of typhoid bacilli are inversely proportional. The following table,* compiled by Mr. Caink, engineer to the city of Worcester, England, will now show the proportion in which the disease occurs according to each class of water-supply.

*Article on Typhoid-fever, Encyclopedia Brittanica.

Occurrences of Typhoid According to Sources of Water Supply.

Source of Water	Town	Annual Typhoid case-rate per 100,000.								
		1892	1893	1894	1895	1896	1897	1898	1899	1900
Deep wells in Red Sandstone	Wolverhampton ...	109	184	109	146	159	117	124	224	237
	Birkenhead	157	207	185	165	138	126	211	230	145
Deep wells in Chalk	Southhampton.....	145	159	109	83	78	64	153	171	109
Upland Surface Water	Liverpool	152	275	267	190	168	160	129	149	115
	Manchester	120	120	90	96	92	90	118	78	78
	Plymouth	126	63	47	32	31	49	41	49	120
Rivers (Filtered)	London	65	84	77	81	71	70	66	98	95
	Reading	30	35	28	53	30	67	32	48	41
	Worcester	155	145	110	36	43	45	31	50	26

A study of these figures renders it apparent that with regard to the causation of typhoid-fever the potency of ground-waters is much greater than that of surface-waters. Heretofore ground-waters have been considered the most desirable source of water-supplies, while surface-waters have been regarded with suspicion, yet, with respect to typhoid-fever, the evidence shows that ground-waters are the more dangerous. If the prevalence of typhoid-fever as represented by the figures in the above table is measured by the relation of protozoal organisms to typhoid bacilli, it will be found to coincide with the presence of typhoid bacilli in water as determined by those factors which regulate the balance of organic life generally in water.

Some credit may be allowed to improved methods of sanitation for the diminution of typhoid-fever prevalence, but except in so far as it has led to a wider use of reservoir-water it cannot afford a satisfying explanation for the difference in the urban and rural incidence, or for the progressive decrease of the disease during recent years. No method has yet been devised to render public water-supplies free from contamination by typhoid bacilli, and were it not that the wider use of reservoirs allows of greater opportunities for the restraining influence of sunlight and protozoal organisms upon them, there is good reason to believe that the reduction which has occurred during recent years in typhoid-fever prevalence, would be much less apparent. But since this implies an inverse relation between cancer and typhoid fever, it is obvious that *the reduction of typhoid-fever*

prevalence has been gained at the expense of increased cancer mortality.

The inverse relation between Cancer and Typhoid-fever.—The evidence concerning the relation between cancer and typhoid-fever is of peculiar value for the reason that, being entirely statistical it is independent of all theoretical considerations. Statistics represent facts, and if the material upon which they are based is sound, the conclusions derived from them are absolute. It must be recognized, however, that the statistics of disease are never free from certain errors, which, while not sufficient to destroy their value, tend nevertheless to obscure their true meaning: Thus, for instance, the relations of typhoid-fever which it is proposed to consider, concern only those cases of the disease which arise from water, but since statistically these are not distinguished from other cases which arise from direct infection, food, flies, etc., it is obvious that the influence of water is not represented in its true proportion.

In addition to those cases of typhoid-fever which are due to causes independent of water, a considerable number, which arise during epidemics, though they are directly due to infected water, yet, for the reason that their causation is determined by artificial conditions, should be eliminated from consideration in the present connection. The true relation between cancer and typhoid-fever is governed by sunlight and other natural influences, but, more especially with regard to typhoid-fever, modern systems of sanitation have introduced

conditions, which, when reflected in the statistics of these diseases, tend to obscure its meaning. Thus, for instance, an epidemic may follow infection of the public water-supplies, through a leaking drain-pipe or some other defect which is preventable, and therefore in a broad sense accidental. Such an epidemic is always limited to the population supplied by the water-system thus infected, and since defects are liable to occur in all systems, the statistics of typhoid-fever in any such locality are liable to fluctuations which represent the effects of artificial conditions—not the true relation of typhoid-fever to water.

The influences of such local conditions upon the average figures of an entire state or country is minimized according to the proportion which they bear to the whole, and although such averages must necessarily include some factors which tend to neutralize the significance of the relation between cancer and typhoid-fever, yet, even in the face of these, they show unmistakably that over wide areas *high cancer-rates are associated with low typhoid-fever-rates, and low cancer-rates with high typhoid-fever-rates;* or, in other words, that the rates of cancer and typhoid-fever are in inverse proportion.

The progressive increase of cancer, and the corresponding decrease of typhoid-fever in America, are shown in the table herewith. The figures are from the "Fourteenth Annual Report, Bureau of the Census, Mortality Statistics, 1913":

ANNUAL AVERAGE MORTALITY-RATES. U. S. REGISTRATION AREA.

During the period 1900-13, per 100,000 population.

Year.	Cancer.	Typhoid-fever.
1900	63.0	32.0
1901	64.3	
1902	65.1	
1903	68.3	
1904	70.2	
1905	71.4	
1906	69.1	25.6
1907	70.9	
1908	71.5	
1909	73.8	
1910	76.2	23.5
1911	74.3	21.0
1912	77.0	16.5
1913	78.9	17.9

During the period of 14 years covered by the above, the general rate of cancer has risen about 16 points, or 25 per cent., and that of typhoid-fever has fallen about 14 points or approximately 50 per cent. The real significance of the table lies in the regularity with which typhoid-fever varies with respect to cancer. It should be remembered that cancer is usually of long duration, and the figures for any year do not relate to cases contracted within that year, but probably one or two years previously, while the figures for typhoid-fever mostly represent cases contracted in the same year.

The inverse relation between cancer and typhoid-fever is also clearly shown by the mortality-rates of these diseases for each state in the United States Registration Area. The figures as given by the Bureau of Census, but for convenience arranged in order of cancer-rates are as follows:

MORTALITY-RATES OF CANCER AND TYPHOID-FEVER IN U. S. REGISTRATION AREA, 1913.

Per 100,000 population.

State	Cancer Rate	Typhoid-Fever Rate	Ratio of Cancer to Typhoid
General rate U. S. R. A...	78.9	17.9	4.4 to 1
Vermont	111.7	7.8	14.3 to 1
Maine	107.5	12.0	8.9 to 1
New Hampshire	104.4	11.9	8.7 to 1
Massachusetts	101.4	7.9	12.9 to 1
California	97.6	15.9	6.1 to 1
Rhode Island	93.3	8.3	11.2 to 1
New York	87.8	10.3	8.5 to 1
Connecticut	85.1	11.3	7.5 to 1
Maryland	82.8	33.3	2.4 to 1
Ohio	8.18	24.0	3.4 to 1
Michigan	81.5	18.4	4.4 to 1
Indiana	81.1	25.1	3.2 to 1
Wisconsin	78.5	9.0	8.7 to 1
New Jersey	78.4	9.6	8.1 to 1
Minnesota	75.1	10.8	6.9 to 1
Pennsylvania	72.2	18.1	3.9 to 1
Missouri	67.1	24.4	2.7 to 1
Washington	53.5	10.3	5.1 to 1
Utah	52.1	22.2	2.3 to 1
Colorado	50.7	17.0	2.9 to 1
Montana	49.4	22.7	2.1 to 1
Virginia	48.4	33.3	1.4 to 1
Kentucky	48.0	42.7	1.1 to 1
North Carolina	47.9	57.4	1 to 1.1

It is interesting as a coincidence, but without special significance that Vermont has the highest cancer-rate and the lowest typhoid-fever-rate, while in North Carolina the lowest cancer-rate is associated with the highest typhoid-fever-rate.

In the year to which these figures refer, there were 24 states in the Registration Area: if these are divided according to their cancer-rates into two equal divisions, and the average rates of each division be taken, the result will appear as follows:

	Average Cancer Rate	Average Typhoid-Fever Rate	Ratio of Cancer to Typhoid
12 States with Highest Cancer-rates	93.2	14.4	6.4 to 1
12 States with Lowest Cancer-rates	60.1	23.0	2.6 to 1

The foregoing is sufficient to establish the relation between cancer and typhoid-fever in America, but in view of the fact that the prevalence of cancer varies widely in different parts of the world it is necessary to determine whether the same relation is maintained throughout. The following table covers a very wide area and includes the greatest variety of conditions: it is based on figures in "The New Dictionary of Statistics".* The arrangement is in order of cancer-mortality.

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*"The New Dictionary of Statistics," (1911) Augustus D. Webb, B. Sc. (Econ.) F. S. S., George Routledge & Sons, Ltd., London; E. P. Dutton & Co., New York.

Average Annual Death-rates During 1903-7.
Per 100,000 inhabitants.

City	Cancer and other Malignant Tumors.	Typhus and Typhoid Fever.
Lyons	166.5	16.1
Copenhagen	151.9	3.6
Bordeaux	136.5	15.4
Munich	134.2	3.0
Edinburgh	124.2	5.2
Vienna	122.8	3.8
Berlin	112.3	4.2
Milan	112.2	38.2
Paris	111.7	10.2
Stockholm	110.7	2.7
Christiania	109.4	2.3
Amsterdam	109.0	9.8
Dundee	107.2	10.6
Hague	107.9	5.0
Leipzig	106.2	4.7
Elberfeld	105.6	4.1
London	102.1	5.9
Dublin	97.0	16.6
Aberdeen	96.5	4.6
Boston	96.0	18.4
Buenos Ayres	94.9	17.9
Trieste	94.1	16.1
Rotterdam	93.7	11.6
Cologne	93.0	4.5
St. Petersburg	92.2	86.3
Madrid	91.7	54.4
Budapesth	89.8	11.5

City	Cancer and other Malignant Tumors.	Typhus and Typhoid Fever.
Havana	88.3	28.4
Athens	84.4	86.7
Liege	84.2	10.0
Glasgow	84.0	12.4
Ghent	83.7	8.2
Washington	81.2	47.2
Kioto	75.1	23.1
New York	71.9	16.7
Warsaw	71.4	21.0
Rosario	69.1	78.9
Antwerp	68.0	12.7
Osaka	67.4	7.3
Marseilles	66.2	49.3
Brussels	65.8	9.9
Belfast	62.8	31.8
Naples	61.4	11.9
Tokio	59.5	17.9
Potosi	38.8	33.7
Rio de Janeiro	30.1	8.0

There are in the foregoing table 46 cities, the average rates of which are: Cancer 93.0, typhoid (including typhus-fever) 19.7. The ratio of cancer to typhoid in 23 cities with the highest cancer-rates is 11.3 to 1: in 23 cities with lowest cancer rates, 2.5 to 1.

The figures in this table include both typhus and typhoid-fever, but for the broad purpose in view this is not of material importance. The average ratio of cancer to typhoid is 4.7 to 1; which is sufficiently near

to that of the United States Registration Area—4.4 to 1—to prove the absence of any serious discrepancy, and also to show that the relation between cancer and typhoid-fever is universally constant.

The evidence of the foregoing appears to be sufficient to establish the inverse character of the relation between cancer and typhoid-fever, but since it is not limited to any series of figures, it may, if desired, be extended indefinitely. It is for instance annually represented in graphic form in the charts of the "Mortality Reports" of the United States Census Bureau, a study of which will reveal the remarkable fact that though cancer and typhoid-fever vary, with respect to each other, in a regular manner, the variations of all the other diseases represented in the charts are independent. Thus, for instance, there is no relation between the variations of pneumonia, heart-disease, tuberculosis or Bright's disease, or between any of these and cancer or typhoid-fever, notwithstanding that etiologically and pathologically there is apparently more in common between these diseases than between cancer and typhoid-fever.

It has been shown that the nature of cancer is consistent with the view that protozoal organisms are an active factor in its causation, and also that the manifestations of cancer coincide with contact of water at the site of their origin according to the frequency and duration of such contact, and the potency of the water as determined by the presence of protozoal organisms in it.

Further, it is accepted that the cause of typhoid-fever, namely, the typhoid bacillus, exists in water, and

it has been shown that between this bacillus and protozoal organisms in water there is an inverse relation which is governed by the character of the water as determined by its exposure to sunlight, movement, and other natural influences.

Also, it has been shown that *between cancer and typhoid-fever there is an inverse relation which coincides in all respects with the relation between protozoal organisms and typhoid bacilli.*

Therefore, on these grounds it is evident that protozoal organisms bear the same relation to cancer as typhoid-bacilli to typhoid-fever, and since the relation between typhoid bacilli and typhoid-fever is a causative one, there is not less reason to believe that the relation of protozoal organisms to cancer is causative also.

PART IV

It will be remembered that four factors, namely: (1) a living tissue-cell; (2) a lesion exposing living-cells; (3) a fertilizing element; and (4) water, are concerned in the causation of cancer; and since each of these is essential, it is obvious that theoretically the elimination of any one would be sufficient to prevent the disease. From a practical viewpoint, however, it is not necessary to consider more than two of these factors; since, owing to the fact that the first and third are determined by the second and fourth respectively, the problem of cancer-prevention becomes resolved into a question of the means by which it is possible to control the disease through the two factors—lesions and water.

The control of cancer through lesions.—In view of the recently-organized campaign to control the spread of cancer it is interesting to find that, though founded upon empirical observation, the modern doctrine of cancer-prevention is in harmony with the conclusions of theoretical speculation concerning the importance of lesions in cancer-causation. A certain value attaches to the unanimity which exists on this subject, for the reason that, by the union of Experience and Theory a mutually-sustaining force is created, by virtue of which the integrity of each is increased.

The possibilities of preventing cancer through the control of lesions, though theoretically sound, must, however, always be limited by the practical difficulties

involved in the discovery and treatment of lesions which are not easily accessible. For this reason cancer of internal organs is beyond the reach of any means local in its application, and since these comprise the great majority of all cases of the disease, it is evident that the advantages to be gained in this direction are not sufficient to remove the menace to the community.

Sterilization of all water required for contact with the body is an absolute preventive of Cancer.—Since cancer is caused by contact of water containing protozoal organisms with lesions of the body-surfaces, it is obvious that the first and broadest principle in its prevention demands that CONTACT OF WATER IN WHICH ORGANIC LIFE IS PRESENT, WITH ANY PART OF THE BODY, MUST BE AVOIDED. This primary principle insures against every possibility, and in so far as it is rigidly observed, cancer is preventable.

In the application of this principle for practical purposes, it is in effect required that ALL WATER FOR PERSONAL USES MUST BE RENDERED STERILE. But in addition, if the sterile condition is to be maintained it is necessary that provision be made for protection against contamination, and the development of a fresh growth of living organisms. For this reason sterile water must be stored in the dark, in covered receptacles which are capable of being easily and thoroughly cleansed, and from time to time sterilized, and which allow of no contamination from an outside source.

Water may be sterilized by chemical, mechanical, or electrical processes, but it does not appear at the pres-

ent time that any of these are sufficiently reliable or convenient for general use on a scale calculated to produce the best results in cancer-prevention. Developments in the purification of the public water-supplies are possible in many directions, but there is no immediate prospect that water can be delivered to the consumers free from organic life, and consequently adequate means for the sterilization of all water required for personal uses should exist in every household. For general use there is no method of water-sterilization which equals boiling in availability, convenience, efficiency, or simplicity, and it is sufficient for the immediate purpose of cancer-prevention that ALL WATER FOR PERSONAL USES SHOULD BE BOILED.

A strict observance of the principles of cancer-prevention must necessarily involve considerable changes in personal habits, and also in domestic and occupational arrangements, but there is good reason to believe that the inconveniences arising therefrom will be more than compensated for, not only by the removal of cancer from the catalogue of human afflictions, but also by the avoidance of a large proportion of the economic loss due to cholera, typhoid-fever, and other diseases less clearly defined which are recognized to be due to the use of impure water. Owing to the unusual dread of cancer in the minds of most persons it is probable that the disposition to acquire a practical knowledge of the principles of cancer-prevention, with a view to applying it for purposes of protection, will outweigh ordinary considerations of convenience.

For general guidance the main lines of cancer-prevention may be stated briefly as follows:

1. All water for drinking should be boiled, and preferably filtered, to remove dead organisms, though this is not essential. Distilled water, if prepared and stored under proper conditions is excellent. Water treated by any other process should never be used unless its freedom from organic life is reliably assured. Ice which is not manufactured from sterilized water should be avoided.

2. Water for bathing, and all other domestic uses, should be boiled, but filtration is not necessary. Raw water should never be applied to any injured part, and water used for medical reasons should, under all circumstances be sterilized. Should contact of unsterilized water with any part of the body inadvertently occur, the part should be wiped with some suitable material until thoroughly and completely dry. Bathing in fresh-water or sea-water cannot be indulged in without risk.

3. For occupational purposes, sterilized water should be used where possible, failing which, some means of protection must be devised, according to the nature of each occupation.

The daily consumption of water in cities ranges from about 30 to 300 gallons per head, and although only a proportion of this is used for personal and domestic purposes, yet the quantity consumed in an average household is far in excess of actual requirements, and

might, without any sacrifice of personal or domestic cleanliness, be considerably reduced. When the necessity for sterilization becomes generally recognized, there will be a tendency, for reasons of economy, to adjust the use of water so as not to exceed the limits of actual needs, and when this point is reached it is to be expected that, by intelligent management, it will be possible to sterilize the quantity required by means of the existing household facilities. Improved methods are possible, and doubtless will be adopted when a demand for them arises; in the meantime it is sufficient that the means of cancer-prevention is within the immediate reach of every individual.

In conclusion, it may be said that though experimental research may yield results of general scientific value, it can never define precisely the causative organisms of cancer. Cancer is a result of fertilization, and the number of species theoretically capable of causing it is uncountable. But, since fertilization is the most subtle process in Nature, it is extremely doubtful whether actual identification of any organism will at any time become possible. Experiment may in the future verify the general causative relation of protozoal organisms to cancer, but until a point is reached where uniform results are obtained under precise conditions, the negative findings of experiment can have no value whatsoever, and positive findings must necessarily tend to confirm the views herein expounded. There is good reason, however, to anticipate that, similarly to yellow-fever and some other diseases, the disappearance of cancer, in

advance of exact scientific demonstration of its causative agent, will supply the most satisfactory confirmation of the truth of its underlying theory.

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Cancer and water